IL-23, A NOVEL MARKER IN THE DIAGNOSIS OF PSORIASIS

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CERTIFICATE

This to certify that the dissertation entitled **"IL-23, A NOVEL MARKER IN THE DIAGNOSIS OF PSORIASIS"- A CASE CONTROL STUDY** is the bonafide original work done by **DR.G.EZHIL,** Post graduate in **Biochemistry** under overall supervision and guidance in the Department of Biochemistry, Kilpauk Medical College, Chennai, in partial fulfillment of the regulations of The Tamilnadu Dr. M.G.R . Medical University for the award of M.D. Degree in Biochemistry **(Branch XIII)**

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DECLARATION

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CONTENTS

ABBREVIATIONS

IL	:Interleukin
ICAM	:Inter Cellular Adhesion Molecule
VCAM	:Vascular Cell Adhesion Molecule
TNF	:Tumor Necrosis Factor
INF	:Interferon
TGF	:Transforming Growth Factor
CBC	:Complete Blood Count
VEGF	:Vascular Endothelial Growth Factor
FGF	:Fibroblast Growth Factor
KCF	:Keratinocyte Growth Factor
NGF	:Nerve growth factor
GM-CSF	:Granulocyte macrophage colony stimulating factor
G-CSF	:Granulocyte colony stimulating factor
CNTF	:Ciliary neurotrophic factor
JAK	:Janus kinases
STAT	:Signal transducers and activators of transcription
MIP	:Macrophage Inflammatory Protein
MCP	:Monocytes Chemoattractant Protein
DC	:Dentritic Cells
KC	:Keratino Cytes
HLA	:Human Leukocyte Antigen
IP-10	:IFN Inducible Protein -10
TCR	:T Cell Receptor
TLR	:Toll Like Receptor
CD	:CLUSTER Of Differentiation
DALY	:Disability- Adjusted Life Year

YLD :Years Lived With Disability

YLL :Years Of Life Lost

RUNX 1 :Runt Related Transcription Factor

ROS :Reactive Oxygen Species

NOS :Nitric Oxide Synthase

NO :Nitric Oxide

ROR :Retinoic Acid Receptor Related Orphan Nuclear Receptor

APC :Antigen Presenting Cells

LFA-1 :LYMPHOCTE Function Associated Antigen-1

CAD :Coronary Artery Disease

PSA :Psoriatic Arthritis

MS :Multiple Sclerosis

IBD :Irritable Bowel Syndrome

SLE :Systemic lupus erythematosus

DM :Diabetes Mellitus

HT :Hypertension

CAD :Coronary Artery Disease

INTRODUCTION

One of the most common dermatological problems is inflammatory skin diseases. They occur in various forms, from acute infrequent rashes in unison with skin itchiness and redness, to chronic forms such as psoriasis, seborrheic dermatitis, dermatitis (eczema), and rosacea. In these inflammatory diseases, psoriasis is a common, chronic, mutilating, inflammatory, and proliferative condition of the skin. In psoriasis both genetic and environmental influences have a crucial role[38].

To understand the pattern of psoriasis, many studies are done recently. This recent progression shows that the local and systemic cytokines regulation contributes an important role in pathogenesis[3].

Psoriasis occurs in global. It affects almost the entire age irrespective of women and men, in all countries, despite the consequences of racial origin[78]. In 1979 to 2008, the scrutinisation of the global trends in prevalence shows that existing prevalence has greater than before from 4.8% to 11.4% [78], but it is middling about 4.6% in developing countries as per Parisi.R et al studies[21]. But in majority of contribute, prevalence ranges 1.5 and 5% in developed countries. There are more evidences to put forward that the psoriasis prevalence is in a rising condition [78]. The prevalence of psoriasis in India is 0.44 to 2.8%. The point prevalence is 8%. [20]

Psoriasis is considered equally prevalent in both sexes[78]. To compare with males, the age of occurrence is younger in females. But there is a

significant difference present in the age of onset. It appears as bimodal distribution of the age of with two peaks in the occurrence – the first peak is from 16 to 22 and the second one is from 57 to 60 years of age. It also occurs in children[76].

In some families, psoriasis runs more frequently. 41% risk of child developing psoriasis if both parents are affected, if one sibling is affected it is 6% and if one parent is affected the risk is 14% [21].

Most common representation of the disease is reddened erythematous, scaly, sharply demarcated, indurated skin plaques, frequently with itching, stinging and irritation[4,22,76]. Psoriasis can occur anywhere on the body, but the scalp, face, palms, elbows, knees, legs, lower back, and soles of the feet are chiefly affected sites[23]. It is present in different types of morphological appearances such as seborrheic, geographic, exfoliative, eczematous, pustular, rupoid and guttate [38].

The etiology is local hyper proliferation and increased turnover of KCs due to climatic change, particularly the winter season and the angiogenesis, induced by proangiogenic cytokines VEGF, IL-8 was first thought to be the reason.

Later then some other studies suggested that the pathogenesis is due to the vital participation of keratinocytes, natural killer cells, macrophages, T cellsand antigen presenting cells and natural killer cells[3,58]. Lastly it was hypothesized that it is an immune mediated disorder with cutaneous and

systemic over expression of a number of proinflammatory cytokines; most predominantly type-1 cytokines for example IL-2, IL-6, IL-8, IL-12, IFN-gamma and TNF-alpha. After the detection of IL-23, this conclusion was challenged and then experimental and clinical facts put the center of attention on the IL-23/Th17 axis in psoriasis [5].

Now the conclusion is, for the initiation, maintenance and recurrence of skin lesions is attributable to over expression of these proinflammatory cytokines especially the IL-23/Th 17 axis. As well the keratinocytes hyperproliferation and the composition of inflammatory cells inside the plaques are also to be headed by cytokines[3,4,75].

As per Fotiadou et al study, IL-23, IL-17A, and IL-22 plays a crucial role in the activity of psoriasis and the early stages of the disease. These cytokines levels are when compare with the stable disease shows a significant increase in active disease[15]. IL-23 highly significantly negatively correlated with disease duration[1].

Like other noncommunicable diseases, Psoriasis affects the quality of life to a particular degree[21]. As compared with other skin inflammatory diseases, they have greater percentage of comorbidity for example coronary artery disease, arthritis, metabolic syndrome consist of diabetes mellitus, dyslipidemia, and hypertension,. [78,67.]

Patient may experience considerable physical discomfort and disability depending on the seriousness of the disease and site of skin lesions.

Itching and pain can disturb the day today life activities like, self-care and sleep. Certain occupations and participating in some of the sports and mingling and engaging with family members and others can be prevented by these skin lesions. Some individuals may feel poor self esteem leads to depression and anxiety [16,21]. Epidemiological studies also have shown that an increased standardized disease mortality in patients with psoriasis, particularly related to cancer and heart[16].

The diagnosis of psoriasis is usually based on the presence of typical skin lesions. And rarely the biopsy is needed.[21] Serum IL-10 and IL-23 levels were notably raised in active psoriasis patients, indicates their role in disease pathogenesis and IL-23 negatively associated with extent of the disorder.[1]

Right now there is no cure for psoriasis. So many researches are underway for better treatment and possible cure. Major thing to improve lives of patients with psoriasis is knowledge and wakefulness about the disease and treatment[107]. In these some works currently leads to molecular therapeutic aspect.

In this way, the aim of the study is to assess the IL-23 levels in early cases. By the IL-23 level, in future can cure or prevent the comorbidities and mortality in the patients or the person with a family history of psoriasis.

AIM AND OBJECTIVES

AIM:

To assess the level of IL-23 in psoriatic patients.

OBJECTIVES:

- To assess the level of IL-23 in psoriatic patients and healthy individuals.
- To compare the IL-23 level in psoriatic patients and healthy individuals

REVIEW OF LITERATURE

DEFNITION:

Psoriasis is a chronic, common, noncontagious, inflammatory, proliferative, disfiguring condition of the skin. It is stigmatizing skin disease together with profound impaired quality of life, having genetic and environmental impact in main play. The mainly distinctive lesions consist of sharply demarcated, indurated, scaly, red plaques. Over the scalp and extensor surfaces these plaques present predominantly.

The degree, periodicity of flares and duration is variable in each patient. Frequent morphological variants are also seen.[76]. Psoriasis is not spreaded by physical or sexual contact. Lifestyle, diet, or bad hygiene is also not the cause for psoriasis.

HISTORY OF PSORIASIS:

Psoriasis was a known word only from the second century, before that no such term was used by the people. By 19th century there was clear relationship between psoriasis and articular symptoms were recognized[36].The terms psora and lepra was used for diseases that can be recognized as psoriasis by Hippocrates. Later Willan named it, discoid lepra Graecorum and psora leprosa in thought of two distinct form of psoriasis. But these two variants were pointed out the one disease, i.e. psoriasis was implied by Ferdinand Von Hebra the Viennese Dermatologist [57]. The psoriatic arthritis was first described in early 19th century.

INCIDENCE AND PREVALENCE:

For the incidence of psoriasis, only few studies are there. Evocative reliable datas are difficult to find because of there is no compulsion for registration of cases of psoriasis in hospitals. In 3 countries Morocco, Algeria and Tunisia, a 14 days psoriasis screening study was performed parallel in 2012 to know the incidence. The projected psoriasis incidence are correspondingly15.04, 10.36 and 13.26 [78,45].

Worldwide psoriasis is a common disease. In most of the countries apart from of ethnic origin, men and women of all ages are affected. The psoriasis prevalence from a variety of numbers of studies it is evidence for a discrepancy between 0.09% and 11.4% among all countries. Prevalence is around 1.5 and 5% in developed countries generally. There is a steady state increase on the prevalence of psoriasis is suggested by some studies [78]. Population prevalence is of 1.5-3%[4]. The prevalence in south India was only 2.8% [20].

In clinical category, the frequently occur one is chronic plaque psoriasis (50%) . In descending order, the quotient of involved sites were the trunk, limbs, scalp, face, palms-soles and flexures.30% shows worsened clinical picture in winter season. [39]

AGE AND SEX DIFFERENCE:

The onset of psoriasis stands for a constant lifelong risk. Any age can develop the disease[64]. It has a diagnostic problem as well as has insurmountable clinical representation even in neonates but incidence among neonates is rare.[66] 1.1: 1 is the male female ratio in the psoriasis patients. Highest prevalence was noted in the age group of 21-30 and 41-50 years, comprising 25% each. [39]

SEASONAL INFLUENCE/CLIMATIC GOVERN:

Cool temperature, dusk, and low moisture of wintry weather trigger the blazing of psoriasis. This type of climatic oversee can augment skin permeability, epidermal thickening, and arouse inflammatory mediator assembly[8]. The deterioration of severity in summer may be attributed the immunomodulatory and bactericidal effects of the sunlight. [8, 96]

FAMILY HISTORY:

Lower numbers of family history was account by the Indian studies. 14% of positive family history was reported by Bedi in his study. While only 2% of family history was accounted by Kaur *et al*. 84% affected in First degree relatives while 12% of cases in second degree family relatives. In psoriasis family history, barely minimal studies are done, so the specific statistical figures on familial incidence is not available [39].

MODE OF INHERITANCE:

Probability of a positive family history and earlier onset is greater [104]. Various researchers agree that genetic basis take part as an etiologic role, for the prevalence of psoriasis in family's leads to the guess that there is no conformity on the mode of inheritance. The elucidation of the observations ranges from simple dominance to digene recessivity. [94,83]

The elemental theories of the form of inheritance of psoriasis are:

* Autosomal dominant with incomplete penetrance;

* Double autosomal recessive;

* Multifactorial[94].

Genomic imprinting proposes an epigenetic effect that is, based on the sex of the transmitting parent, the degree of difference in expression of gene occurs. A non-mendelian mode of transmission has also been proposed for psoriasis and PsA by genomic imprinting.[84, 83]

In genetics of psoriasis this is evidenced most convincingly by the report that, 63% concordance among identical twins versus 15% concordance among dizygotic twins. The risk for offspring is 14-15% if one parent is having psoriasis, and it is 41-75% if both parents are involved. The risk of subsequent children is 6-20% if neither parent has the disease but the child affected [89].

In P Rahman et al study, the sex of the parents with psoriasis has effect on the birth weight of the offspring. That is, with offspring of males with

psoriasis weigh 270 g more than offspring of females with psoriasis. The same authors reresearched the same population in the Faroe Island and documented that a higher penetrance of psoriasis if the male parent was presumed gene carries or was affected [84].

GENETICS:

IL 23A gene codes for the IL-23p19 subunit has recently been found as proof for the genetic association with psoriasis.A familiar risk haplotype was recognized in IL-23R receptor gene, at 310 aminoacid proline, and at 381 aminoacid arginine . In IL-23R, at 381 position if change the glutamine for arginine then it is establish, it would be defensive against psoriasis. IL-12Rβ1, IL-12Rβ2, p35 and p19sites polymorphism was not complexed with psoriasis vulnerability in these studies[35]

In sibling pair analysis, it is confirm that chromosome 6p has the liability gene for psoriasis. They ascertained out that there is a strong linkage to replication loci on chromosomes 17 and 4, once the allele was of paternal origin, and was most considerable one in those families without psoriatic arthritis[83].

GENETIC STUDIES:

Within the past decade, on the basis of genome-wide linkage studies, several putative loci for genetic susceptibility to the disease have been reported.

They found out one locus in the major histocompatibility-complex (MHC) region on chromosome 6 has been replicated in several populations[91].

It is most commonly stated that HLA-Cw**6**, HLA-B13, HLA-Bw57 and HLA-DR7 are the HLA types associated with psoriasis. 50% percent of psoriasis cases coupled with PSORS1 gene[91, 110]. Homozygotes for HLA-Cw0602 have 2.5 fold advanced risk of having psoriasis in compare with heterozygotes.[64]

TABLE 1: Genetic susceptibility loci in psoriasis [66, 91,76]

Location	Position	concerned Genes
PSORS1	6p21.3	Corneodesmosin, HCR
PSORS2	17q25	
PSORS3	4q	
PSORS4	1q21	Epidermal differentiation complex gene cluster
PSORS5	3q	SLC12A8
PSORS6	19p	
PSORS7	1p	

Most recently it has been revealed that an extra gene locus for psoriasis liability was on chromosome 17q25. This locus is a runt-related transcription factor 1 (RUNX1) binding-site variant, encodes for a gene implicated in the growth and of blood cells, plus cells of the immune system.[91]

GLOBAL BURDEN OF PSORIASIS:

In 2010, to evaluate the degree of dissuade or dearth of healthiness owing to diverse diseases was assessed by 'The Global Burden of Disease Study'. The Disability -Adjusted Life Year (DALY) in one of the metrics frequently used for this assessment. The whole total of and years of life lost (YLLs) and years lived with disability (YLDs) is equaled to DALY. One lost year of a healthy life is meant to be one DALY. .

DALY = YLD + YLL **1 DALY = 1 lost year of healthy life**

In psoriasis the scrutiny of the Global Burden of Disease Study suggested that the burden is high-pitched. For psoriasis at 2010, the global average of DALY was estimated 1050660, which is twice in so far as for acute hepatitis C [12, 78].

HISTORY OF PATIENTS:

The foremost symptom is generally pruritus and disturbed sleep is encountered by the majority of the patients. In unstable pustular or erythrodermic psoriasis, the common features are skin tightness and burning of the skin. In palmoplantar or flexural disease pain may be encountered in areas of fissure formation. In scalp psoriasis, peeling of scale from the lesion is a major symptom.

At any age first sign of psoriasis may appear and in common those with have a family history of psoriasis, sooner the onset disease are more likely to. Amongst the individuals the course of disease as well as the occurrence of

relapses and remissions varies to a particular extent. The degree of involvement of specific sites by psoriasis that may not be expressed by the patient, for example the ano-genital region it is essential to ask about [67].

Table 2: Different morphology of psoriasis[57]:

Different types of morphologic features	
1. Generalized	2. Serpiginous
3. Follicular	4. Inverse
5. Pustular	6. Geographic
7. Annular	8. Guttate
9. Nummular	10. Gyrate

PRESENTATION:

The typical lesion is a well-demarcated from normal skin, sharply declined edges, itchy, pink to salmon-colored plaque covered by slackly adherent scales that is typically silvery white in color[21,34,65,67]. There is silvery or yellow white scaly lesion similar to mica [66]. Some lesions are presenting as annular, linear, gyrate, and serpiginous like different configurations [65]. A clear peripheral zone encircles the plaques called, the halo ring of Woronoff.

NUMBER: Number of lesions may be several to single one. From one to several centimeters, the diameter differs. On the legs and sacral region it is commonly seen that the formation of coalescence of smaller plaques into large plaques. Involuting lesions often clear from the center initially, producing annular or arcuate shapes.

HISTOLOGICAL APPEARANCE:

In early budding lesions vasodilatation, papillary edema and leukocytes infiltration pave the way to the epidermal changes. Following this compact hyperkeratosis, disappearance of granular layer and slight epidermal hyperplasia will be continued[76].

Acanthosis (augmented epidermal cell turnover leads to distinct thickening in epidermis) with uniform rete ridges descending extension and appearance of mitotic figures in keratinocytes [64,76]. The stratum granulosum is frailed or not present and widespread parakeratotic scale is visualized.

Characteristic plaque, the majority portion of epidermis is shrunken particularly overlying the dermal papillae (suprapapillary plates). Inside these papillae, circuitous, dilated blood vessels can be seen. This assemblage of changes costs in unusual closeness of vessels within the dermal papillae to the overlying parakeratotic scale, and accounts for the typical clinical occurrence of multiple, minute, bleeding points when the scale is moved up from the plaque(*Auspitz sign*)[64].

Neutrophils form small compilation within the parakeratotic stratum corneum which is called as *munro microabscesses* and inside the spongiotic foci of the superficial epidermis is known as *spongiform pustules*[64].

Histologically there is mixed dermal infiltrate, including $CD4^+$ T cells, dentritic cells, macrophages and mast cells present along with distinct epidermal hyperplasia and parakeratosis [10].

In a plaque lesion, the bulged endothelial cells are activated with having intracellular Weibel-Palade bodies and prominent Golgi apparatus. Dermal blood vessel dilatation and widening of intracellular spaces occurs because of this. For easy migration of inflammatory cells like macrophages etc into the skin, these lesional capillary loops express E- selection, present inside the lesion having venous structural similarity, bridged fenestrations, put up it easier[58,81].

LATENT PSORIASIS:

It is a state which appears before the manifestation of the signs of clinical psoriasis. During this period may be a few aberration present but there is absence of clinical manifestation or the extinction of some hidden defect. This latent stage may possibly occur at birth or later. No consideration of the age at which psoriasis appears, the clinical phase can come into view from the latent stage at any time. The changeover to clinical psoriasis from latent one mostly presents as stable form which waxes and wanes in severity, but infrequently transfer back to the latent period. These switchovers are "natural" in that no treatment brings them about. It is evident that the progression of clinical psoriasis often depends upon one of the "triggering stimuli" or whether it appears to develop instinctively[38].

PATHOGENESIS:

It is seem to be multifactorial, whether symbolize the immune system or the principal disease of skin, or the immune system, or contributions from genetic and environmental factors is being discussed for some years.[1,58,64]

ROLE OF OXIDATIVE STRESS:

Recently some theories have been proposed the participation of oxidative stress in the pathogenesis of psoriasis. Oxidative stress is unevenness among oxidants and antioxidants in favor of the oxidants. This imbalance leads to interference in the redox signaling and control and/or molecular damage[60]. First it has been suggested that there is a compromised function of antioxidant system and increased reactive oxygen species (ROS) production [34].

As it is constantly exposed to UV and other environmental stresses, skin is a vulnerable target for oxidative damage and producing ROS [34]. The nitric oxide synthase (NOS) expression is seen in keratinocytes the major composition of epidermis and fibroblasts in the dermis. Following the UV exposure these above mentioned cells liberated NO which plays a considerable role in immunosupression and erythema and [61]. Increased $NO^{\bullet}$ end products has important role in etiopathogenesis of psoriasis[34.] ROS mediated oxidative damage causes a notable raise in arachidonic acid, DNA modification, and secretion of inflammatory cytokines. Lipid peroxidation of plasma membrane of psoriatic skin cells occurs due to ROS related oxidative damage. [34].

IMMUNOPATHOLOGY[57]:

Most important hints of participation of immune system in pathogenesis:

1. The occurrence and emergence of abundant activated T cells in active psoriatic lesions.
2. Immune mediated emergence of adhesion molecules on the surface psoriatic keratinocytes.
3. The relative absence of T_H2 related skin disorders, for example utricaria and atopic dermatitis.
4. Lymphokine profiles signifying a T_H1 disarray.

INFLAMMATORY MARKERS:

The picture of psoriasis is thought that extremely increased rate of epidermal production, along with set off mononuclear infiltrate in the dermis beneath the affected epidermal layer[3].Then subsequently following cells and cytokines have been thought to take part as vital role in the pathogenesis, that includes; Keratinocytes, Natural killer cells, Langerhans' cell, Antigen-presenting cells, macrophages and T cells. The assembly of Th1 type cytokines, growth factors like keratinocyte growth factor (KGF) and vascular endothelial growth factor (VEGF) and etc [58].

There is unusual expression of antigens such as heterodimers keratin 6–keratin 16 and heat-shock proteins and also the TGF-α, along with hyperprolferation. The TGF-α is an autocrine mediator as well as a master

cytokine significant to disease processing, present in psoriatic epidermis, was evidenced by in vitro and in vivo researches. In adding up, there are intercellular adhesion molecule 1 (ICAM-1) and provoked expression of MHC class II antigens[91,57].

Primary source for angiogenetic activity in the growing plaque is epidermal keratinocyte proangiogenetic cytokines like VEGF and IL-8. Blood vessels that are present psoriatic lesions have features like dilated and knotty, entering directly in the dermal papillary vicinity, beneath the epidermis. ICAM-1 (CD54), E-selectin (CD62E), vascular-cell adhesion Molecule 1 (CD106), and MHC class II antigens, all are uttered by the lesional vascular cells shows the activation [91].

Recent progress in understanding the important role of T cells in pathogenesis of psoriasis is going on. Along with INF-γ and other above mentioned cytokines, the T helper-1 cells dominated cytokine milieu also accounts for the skin lesions.

Current evidences suggest that IL-23 might be a key cytokine in psoriatic lesion. INF-γ production and proliferation of memory Th1 cells are stimulated by IL-23. IL-23 would maintain a Th1-committed memory response by the constant propagation of memory T cells [6].

Table 3: Cytokines in the pathogenesis of psoriasis

CYTOKINES	ROLE IN PSORIATIC PATHOGENESIS
IL-1	Promotion of ICAM-1, VCAM-1and E-selectin on keratinocytes; Emergence of GM-CSF and KGFKGF in fibroblasts; Involvement in angiogenesis.
IL-2	Provoke NK cell activity and T cell cytotoxicity.
IL-6	In dermal infiltrate, boosts up the activation, proliferation of T cell.
IL-8	Into epidermis repositions the neutrophils and T cells; T cell activation and proliferation: Firing up of angiogenesis.
IL-12	Helps in type I T cell maturation pathway; Accelerates the T cell activation.
IL-17	On the surface of fibroblast augments the expression of ICAM-1.
IL-22	Improves keratinocyte mobility by induces MMP, S100, defensins synergistically with IL-17.
IL-23	Core persuader of Th-1 cells and triggers the transcription of nuclear STAT-3; Guides to an increase the level of IL-17 & IL-22; Causes diverse infiltration and distinct acanthosis.
TNF-α	Arouses the synthesis TGF-α, IL-8, PAI-2, ICAM-1, GM-CSF and β-defensins by keratinocytes: Accelerate the endothelial cells to produce VEGF.
INF-γ	APC activity acceleration.
Endothelin- 1	Chemo-attractant to neutrophils; It is mitogenic to keratinocytes; It’s serum level is parallel to severity of psoriasis.

Table 4:Growth Factors

Growth factors	Role in psoriasis
GM-CSF	Speeds up the keratinocyte proliferation and triggers the neutrophils. Invigorates the proliferation and maturation of endothelial cells.
EGF FAMILY	In psoriasis augments the expression of amphiregulin and TGF-α.
VEGF	Causing erythema by up regulation in psoriasis. homogenization of remodeling and growth of vascular cells in psoriasis lesions.
FGF	Presents in both suprabasal and basal layers of the affected lesional skin. Has angiogenic and mitogenic property.
NGF	Over-expression in psoriatic lesion; Quickens endothelial cell and keratinocyte proliferation; Adherence molecule expression; A striking up-regulation of tyrosine kinase A, p75 neurotrophin receptor and NGF receptors.

ROLE OF ICAM IN PSORIASIS:

Intercellular Adhesion Molecules (ICAMs) found in psoriatic plaques in a significant quantity are otherwise known as adhesion molecules. It includes ICAM-1, ICAM-2 which are along with VCAM-1, make availability of costimulatory signals obligatory for T-cell activation by assists the binding of T cells to antigen-presenting cells and keratinocytes. The interactions among cellular adhesion molecule facilitates the continuous recirculation of T lymphocytes among lymph nodes, tissues, and blood [18].

LEUKOCYTE FUNCTION–ASSOCIATED ANTIGEN 1 (LFA-1):

LFA-1was recognized in humans in 1982. Tthis is the element of the leukocyte β2-integrin family of adhesion molecules. Heterodimer shares a common β chain (CD18) and a unique α chain (CD11a for LFA-1).Expression of LFA-1 is constrained to leukocytes.

LFA-1 is an integral molecule in T cell activation and leukocyte trafficking. LFA- 1 interrelates chiefly with ICAM-1, and too intermingles with ICAM-2, ICAM-3 as well as JCAM-1. Memory T cells expresses LFA-1 in higher concentration compared to naive T cells. The b2 subunit of LFA-1 has been drawn in as important for signaling actions thought to be associated with this LFA-1-ICAM-1 engagement. Early studies recommended that great increase in the functional gluttony of T cell:APC interactions is by the primary role of LFA-1[13].

IL-23:

In 2000 during, searching for the members of IL-6 family, IL-23 was discovered by Oppmann and colleagues[40,19].

This is discovered in 2000, more or less 15 years back, IL-23 has promptly shifted as a key player, and a probable therapeutic object in psoriasis than just a pro-inflammatory cytokine.[5] IL-23, IL-12, IL-27 and IL-35 are belongs to the IL-12 family which is wholly are heterodimeric cytokines. Even though are having several structural similarities in the cytokines, downstream signaling components and receptors, they all are

differ in their biological activities. In the development of Th1 and Th17 cells, these two IL-12 and IL-23 play a role of predominant proinflammatory/ prostimulatory cytokines which contribute to the above respectively[14]. IL-23 is a heterodimeric cytokine, consisting of a unique IL-23p19 subunit [5,40]. Belonging to the same family, IL-23 and IL-12 share a common p40 subunit[6].

Synthesis: It is mainly synthesized by activated myeloid cells, epithelial and endothelial cells[5]. In monocytes, monocyte derived dentritic cells(DCs) ,and in mature DCs IL-23p19 in strongly expressed and mainly localized in papillary dermis[19]. In psoriasis, dentritic cells and keratinocytes mainly produced IL-23[5,41,42].

IL-23, through TNF-α and IL-20R2 arbitrates epidermal hyperplasisa, hyperkeratosis, acanthosis and orthohyperkeratosis[47].

Structural relationship between IL-23 and IL-12:

IL-12 and IL-23 are unique because of the way of secretion as binary complexes[82]. IL-23 comprises unique IL-23p19 and IL-12/23p40 [2] and IL-23p19 is most closely related to the IL-12 p35 subunit[5].

IL-12 and IL-23 are heterodimeric typical four-helix cytokines. They are secreted as a complex with a common binding protein termed p40 and a disulfide-linkage linking the helical cytokines p19 and p35. Because of together p35 and p19 have sequence homology to G-CSF and IL-6, both the two are belongs to the members of the glycoprotein (gp) 130-class of long-chain cytokines. The p40 subunit structure resembles the class I cytokine

receptors such as the non-signaling alpha receptors for IL-6 and CNTF. In essence, soluble α-receptor subunit which represented by IL-23 and IL-12 is constitutively associated with the class I cytokine receptors. [82].

In compared to nonlesional skin, the psoriatic skin lesion has increased level of both p19 and p40 mRNA shows a clear cut indication that elevation of IL-23 and its involvement in pathogenesis of psoriasis [35].

Based on their common subunit use of p40, these ILs are important for cell-mediated antimicrobial and cytotoxic activities that is T helper (Th) 1-type responses by this it seems that these two cytokines would have superfluous roles in immune homeostasis. Later,it was hastily exposed that the functions are non-redundant[82].

The relative restricted expression of p40 subunits limits potential IL-23 producing cells to monocytes, macrophages and dentritic cells. The receptor complex for IL-23/12 is expressed or up regulated on T and NK cell and myelomonocytic lineage including DC. The immune response of both IL-23 and IL-12 are comparable, but distinct.IL-12 mainly stimulates the IFN-γ production in naïve T cells. Production of memory Th1 cells and IFN-γ synthesis is better stimulated by IL-23[6].

Functional difference between IL-23 and IL-12 in psoriasis:[2,9]

- IL-23 signals through IL-23R and IL-12Rβ1, while IL-12 signals through the IL-12Rβ1 and IL-12Rβ2 subunits.

- IL-23 accelerates the JAK-STAT pathway activity but acts largely on STAT3 and IL-12 of JAK2 and TYK2 pathway leads to phosphorylation of STAT4 and other STAT molecules.
- . IL-23 brings on IL-17A, IL-17F activity and/or IL-22, and stabilizes Th-17 cell but IL-12 promotes the synthesis of IFN-γ, which is needed for the progression of Th1 immune responses [2,9]**.**

IL-23/ Th-17 AXIS:

In past years major advances in understanding of psoriasis from genetic, immunological and clinical findings, all unambiguously converge on the pivotal role of the IL-23/Th17 axis[5,19].

The pathophysiology of psoriasis can be divided into two discrete immune-mediated phases:

- **Initial Phase**
- **Amplification Phases.[11,59]**

- **Initial phase**:

Resident dentritic cells and keratinocytes perturbation by trauma and/or the following stimulation of pattern recognition receptors (e.g. dectin-1, TLR-2, and TLR-4) in a genetically prone skin lead to stimulation of the innate immune system. This cataclysm of macrophages, dentritic cells and diverse cytokines triggers the production of IL-12 and IL-23[35].

- **Amplification phase**:

By the adaptive immune response, these two cytokines make the bridge from initiation to the amplification phase[11,59]. But this leads to persistence and proliferation of Th17 cells inside the lesion. Following this Th17 cells may enter into the skin, and expression of chemokine receptors, was recently explained [35].

Th17/IL-23pathway promotes chronic inflammation[11]. And this pathway adds to the complexity of psoriasis pathogenesis and provides targets for newer drug development [11]. IL-23 attaches and signals by means of its heterodimeric complex receptor compiled of subunits IL- 23R and IL-12Rβ1. IL-23R is an exclusive in IL-23Rcomplex. IL-23R expresses at memory T cells, DCs, natural killer cells and monocytes.[43,44,45].

IL-23 is implicated in propagation of memory T cells, when compare to naïve T cells which does not responds to IL-23 due to minimal expression or no subunit of IL-23R. IL-23 is responsible for differentiation and expression of Th17 cell population which is exemplified by the synthesis of the IL-17A and related proinflammatory cytokines[19,17,40,46].

IL-23R is acquaintance with Jak2. Stimulation of IL-23 is directed to ligand induced transphosphorylation and autophosphorylation of Jak2. Activated Jak2 in sequence phosphorylates the tyrosine molecules situated in the receptor subunits intracellular domain. Activator of transcription (STAT) and signal transducer molecules tie up with the docking sites of phosphorylated

tyrosine residues. After tying up, phosphorylation of these molecules occur. Now in IL-23 signaling pathway, these above mentioned molecules particularly STAT3 acts as the main participant[19,43].

For Th17 cell development, activation of STAT3 and involvement of the orphan nuclear receptor RORα, aryl hydrocarbon receptor and the Transforming growth factor-β1(TGF-β1) are needed[19,35]. Phosphorylated STAT-3 particles dimerizes from two identical monomers and transfer into the nucleus, invoking cytokine transcription, like IL-17A, IL-17F, IL-22 and INF-γ. Aminoacid switching, in the IL-23R subunit that is, arginine to glutamine and leucine to proline, confer protection against psoriasis.IL-23 thus promotes the IFN-γ production and type-1 immunity[9].

The term "type-1immunity" relates to a environment enhanced natural killer (NK) activities and distorted towards cytotoxic functions of TH1, CD8+ T cell and. The major function of type 1 immunity is to execute intracellular pathogens or cancer cells. Many tissue destructive inflammations for which firstly TH1 cells were blamed, but in reality it is mediated by TH17 cells. Immunopathology, tissue damage and disease onset is due to uncontrolled type-1 cellular immune responses[9].

TH-17 CELLS DERIVATION:

T cells:

70- 80% of blood cells lymphocytes comprise T cells. They have a specialized cell receptor known as 'T cell receptor' (TCR). The main function

of TCR is recognition of antigen. It can act in response to only an antigen which is processed and presented by the macrophages like antigen presenting cells.

TCR: (T cell receptor)[57]

CD4+ T cells migrate into skin causing aggravation of disease and presenting as a new lesions. As compared with T cells of peripheral blood or normal skin, CD4+ T cells on psoriatic lesional skin showed significant greater presentation of Vβ2, Vβ5.1 and Vβ6 T cell receptor. The CD4+ T cells are the majority of T cells localized in the affected dermis, whereas those migrating into the epidermis are predominantly CD8 killer cells. The lesional CD8+ cells have constant oligoclonal expression of Vβ3 and Vβ13.1 T cell receptors. These T cells are activated and expressed in high levels of MHC class II molecules and CD25, IL-2.

Most TCR comprise 2 chains- α and β.TCR does not have α/β and γ/delta chains. TCR is active only when both the chains (α and β), complex with CD3 molecules.

Factors promote the T cell migration into lesional plaque:

The above mentioned receptors in the papillary and dermal endothelial cells receptors guide the T cell to ramble into the lesional skin. This relocation into the psoriatic skin is accelerated by lipid mediators such as 12[R]-hydroxyeicosatetraenoic acid, peptide chemoattractants such as MCP-1, MCP-

2, MCP-3 and IL-8, MIP-1α and MIP-1β, IP10 and as yet other uncharacterized peptides[57].

T cell development:

The majority of important events of T cell development take place in thymus. The progenitor T cells are originated from the bone marrow and then drifted to thymus via blood stream. The chief maturation events take place in the cortex, under the control of thymic hormones and lymphopoietic growth factor IL-17 which are secreted by thymic stromal cells.

The antigen presenting cells differentiate the naïve T cells into Th1, Th2, Th17 or T-regulatory cells by stimulation of the T cell receptor and the fastidious release of cytokines [35].

TH CELLS:

A novel TH subset, has been recently recognized as a distinct TH lineage named as TH_{IL-17}, TH17 or inflammatory TH (THi). Because of secretion of the following proinflammatory cytokines, such as TNF-α, IL-6, from IL-17A to IL-17F, IL-21 and IL-22, it is defined as Th 17 cell [35] .

DEVELOPMENT AND DIFFERENTIATION:

In 2 ways:

1) **IL-23 dependent**
2) **IL-23 independent**

1) IL-23 dependent:

On developing Th17 cells, the generation of IL-23R is by, intracellular signaling through STAT3, RORγT, and extracellular TGF-β. IL-23R upholds the sensitivity of IL-23 as the master cytokine by inducing the continued existence and multiplication of Th17 cells. The IL-23R receptor is a heterodimer made up of IL-12Rβ$_1$, IL23R subunits15[35].

2) IL-23 independent:

The switch from naive CD4 cells to Th-17 cells happens in the presence of IL-6 and exposure to extracellular transforming growth factor (TGFβ) as well as Toll-like receptor-activated monocytes [19]. IL-1β and Tumor necrosis factor (TNF)-α, both these cytokines causes amplification of the Th-17 cell differentiation, which are mediated by IL-6 and TGF-β. The differentiation of the Th 17 cells from naive T cell precursors is also dependent on the intracellular transcription factors RORγ and STAT3[35].

IL-1β was enough for production of both IL-17A and IFN-γ and to create the expression of RORC. In IL-17A-producing cells, a new marker in detected and named as CD161and was recommended as a novel marker for Th17 cells[19,24]

The Th17 differentiation was initiated by TGFβ and IL-6 and mediated by STAT3 via regulating the chromatin remodeling of the IL-17-IL-17-F locus, which is further reinforced by IL-23[49].

Apart from the cytokine induced Th lineage formation, the differentiation is shown to be directly endorsed by the prostaglandin E2. PGE2 synergizes with IL-1β and IL-23 to persuade the up regulation of IL-23R, and IL-1R to promote Th 17-associated profile of transcription factor, cytokine and chemokine receptor expression [50].

Transcription factors comprised in Th cell development:

- IFN-regulatory factor 4(Irf-4)
- Signal transducer and activator of transcription 3 (STAT 3),
- T cell-specific splice isoform of retinoic acid receptor-related orphan receptor (Ror) known as Ror-γt
- Splice isoform of Ror- αd
- Aryl hydrocarbon receptor (AhR)

Cytokines produced by Th-17 cells:

- IL-17A to IL-17F
- Tumor necrosis factor (TNF)-α
- IL-6, IL-22, and IL-26.

IL-17:

TH17 cells produce IL-17A, IL-17F, IL-6 and IL-22, all of which regulate inflammatory responses by tissue cells[49].

It is undetectable in normal skin. It is a member of a newly identified cytokine family comprising IL-17A, IL-17B, IL-17C, IL-17D, IL-17E and IL-17F. IL-17A often referred to as IL-17. Due to close proximity on

chromosome, as well as co-ordinate expression pattern IL-17F shares a maximum homology with IL-17A[50,35].

IL-17RA is uttered on B and T cells, epithelial cells, fibroblasts, monocytic cells and bone marrow stroma. IL-17RA signaling activates both the nuclear factor-kB, and mitogen activated protein kinase intracellular pathways[35].

IL-17 role in psoriasis:

- Proinflammatory activity induces the neutrophils, monocytes/macrophages T cells and epithelial cells to express proinflammatory cytokines, colony stimulating factors and chemokine [16].
- Acts on macrophages to promote their recruitment and survival.
- Conscription and activation of neutrophils via effects on granulopoiesis. [35].
- In inflamed tissue, inhibit the neutrophils apoptosis directly[62].
- It's marked role in sub corneal accumulation of neutrophils and stimulates the production of matrix metalloproteases and aniogenic factors to cause tissue remodeling and angiogenesis.
- CXC chemokine induction.
- Stimulates the mixture of immune and non-immune cells for the synthesis of proinflammatory cytokines and anti-microbial peptides.
- Also enhance the IL-2 production capacity of human CD4+ T cells.
- Enhance the proliferation of both conventional T (T) cells and T_{reg} cells.

Mechanism of action of IL-17:

In psoriasis, the mechanism of IL-17 activity in stems from its co-operative gene regulation IL-22 and other stimuli. Together with IL-17, IL-22 synergistically enhances expression of skin antimicrobial peptides including S100A7 (psoriasin), b-defensin-2(BD-2), and S100A8/9 (calprotectin)[103]. Supporting this, S100A7–9 is elevated in psoriasis, correlating with disease onset. Interestingly as the result of elevated antimicrobial peptide production psoriasis, patients are more challenging to skin infections than non psoriatic people. Another antimicrobial peptide, cathelicidin (LL37), is synergistically increased by treatment with IL-17 in combination with 1,25-dihydroxyvitamin D3. LL37-bound self-DNA fragments trigger TLR9 in DC, which induces a potent adaptive immune response, possibly one of the mechanisms by which self-tolerance is broken[102].

COMORBIDITIES:

Manifestations of psoriasis are not only restricted to the skin. In moderate to severe psoriasis, several other multiple comorbidities also complicate the other systems. Ischemic heart disease, stroke, hypertension, dyslipidemia, obesity/metabolic syndrome, diabetes mellitus, autoimmune diseases, sleep apnea and crohn's disease are some diseases arise in psoriatic people[21,79].

Table 5: The symptoms most often stated by the psoriasis patient [86]:

Symptoms	Descending order of frequency
Skin scaling	92%
Itching	72%
Erythema	69%
Fatigue	27%
Swelling	23%
Bleeding	20%
Burning	20%

ASSOCIATIONS OF PSORIASIS:

Psoriatic arthritis, immunobullous disorder, vitiligo, metabolic syndrome, acne, pustulosis, synovitis and hyperostosis are some clinical entities associated with psoriasis[51].

1. Psoriatic Arthritis:

Arthritis is the most common association with psoriasis was established out by Jean Louis Alibert in 1818. The incidence of arthritis in psoriatic patients is from 1.3% to34.7%. On sex predilection of PsA, there is no proper reliable data. Psoriatic arthritis (PsA) falls under the type of seronegative spondyloarthropathies.

Diagnosis is made with signs of an inflammatory arthritis, presence of skin psoriasis and absence of serological tests for rheumatoid factor[51,52]. Based

on the national psoriasis foundation, up to 30% of the patients have psoriatic arthritis[65.] Usually within 10 years of the onset of psoriasis the PSA affects the joints and occurring PSA after 10 years of onset is low[53]. 27.5% of psoriatic arthritis patients have family history of psoriasis[54].

5 types of psoriatic arthritis;

- Symmetric,
- Asymmetric,
- Distal Interphalangeal Predominant (DIP),
- Spondylitis And
- Arthritis Mutilans.

Symmetric arthritis looks a lot like rheumatoid arthritis, but more often than not is milder. Asymmetric arthritis be capable of involve several joints with the presentation as sausage digits.DIP is classic form, but arises only in relation to 5% of the patients with PSA. Arthritis mutilans is dangerous and deforming. The small joints of hands and feet are affected primarily by this type. Less than 5% of PsA will suffer by this form[65].

2. Obesity/Metabolic syndrome:

The other different names are insulin resistance syndrome and syndrome X. This syndrome includes metabolic abnormalities with high risk of coronary artery diseases and diabetes mellitus. The primary pathophysiology linking the metabolic syndrome and psoriasis engages overlie of genetic propensity and inflammatory pathway. Cytokines, for example IL-6 and tumor necrosis factor-

α dysregulation leads to chronic inflammation interceded by Th-1 and Th-17 cells. . These Th-1 and Th-17 cellsand the cytokines released by these cells persuades epidermal hyperplasia in psoriasis, and alienates signaling function of insulin, intervene the resistance of insulin resistance and change the expression of adipokine, and obesity. Susceptibility to psoriasis or seriousness of disease is due to long term inflammation and angiogenesis and these are promoted by hyperinsulinemia in metabolic syndrome. And moreover, the subsistence of genetic loci, e.g., PSORS2-4, CDKAL1 and ApoE4 and, is too been drawn into the joint of genetic vulnerability of metabolic syndrome and psoriasis. The alliance relating metabolic syndrome and psoriasis is due to the above mentioned shared measures [48].

Different types of surveys has accounted that increased levels of serum immunological markers, like IL-6, IL-2, ICAM-1 and TNF-α , in order to prove that it is a systemic immunological disorder. Inflammation is mainly controlled by hormones and cytokines derived from adipose tissue and liver by IL-1, IL-6 and TNF-α. Common cytokine pathways are responsible for both psoriasis and obesity but it is yet to be answered which pathology comes first when psoriasis-associated obesity and metabolic syndrome is considered [79].

There are so many evidences that prove the relationship between psoriasis and a number of lifestyle factors for example alcohol intake and smoking and other diseases with psoriasis[51].

3. Cardiovascular diseases:

Gelfand et al used the General Practice Research Database (GPRD) to decide the psoriasis is an independent risk factor for myocardial infarction. CAD risk factors prevalence is greater in psoriatic patients. The psoriatic patients with raised TNF-α level has the risk of increased frequency of CAD, pulmonary emboli and cerebrovascular diseases occur [79]. When put side by side to healthy population psoriatic patients had a 1.6 fold increased risk for venous occlusion, 2.6 fold increased risk for other occlusive vascular diseases. Arteriothrombotic markers like fibrinogen and plasminogen activator inhibitor-1 (PAI-1) levels are also seem to be increased in psoriasis[79].

Along with a systemic inflammation, antipsoriatic prescriptions are believed (acitretin, cyclosporine) for the adverse CAD risk factors like elevation of blood pressure, elevation of serum levels of lipids are other possible optional mechanisms for CAD comorbidity of psoriasis .

4. Bullous pemphigoid and vitiligo:

Co localization of vitiligo and psoriasis may be possible because of structural abnormalities between anti stratum corneum antibodies and anti melanocyte antibodies. In addition, a common neuropeptide might be also accountable for co-habitation of psoriasis and vitiligo[51].

5. Psychiatric co morbidity:

Psoriasis causes important adverse effects on the psychological and social aspects of life chiefly due to its visibility. Daily activities, employment

and treatment for disease were most affected physical and psychosocial factors. Sufferers mostly tends to avoid the social contacts because of disturbed feel, low self conscious, live in a constant fear of relapse or bothered by the peeling of the skin.

Patients with psoriasis describe feeling of annoying or defenselessness. They reveal a higher rate of suicidal ideations Compare with other patients, thinking of suicide attempts is in a greater proportion. Among 127 psoriatic patients a study was conducted where about active suicidal thought was reported in 5.5% and “want to die” was 9.7% during the study period[78].

ASSOCIATION WITH PREGNANCY:

Many reports have recommended that physiological changes during pregnancy habitually lessening of systemic and cutaneous inflammatory diseases[88, 89].

In pregnancy, there is a improvement in psoriasis due to hormone mediated down regulation of the immune system. The greatest role in the improvement of psoriasis is played by progesterone. The metabolizing capacity of keratinocyte cells on steroid hormones like estrogen and progesterone also believed to be altered by the hormonal changes of pregnancy. High levels of IL-10 in pregnancy have a favorable effect on psoriasis. In addition, some theories include roles of human chorionic gonadotrophin and human placental lactogen or the possible fetal suppression of the maternal immune system has too some effect on psoriasis[89].

Up-regulation of proinflammatory Th-1 cytokines also plays a key role in the inflammatory streams of psoriasis. It is likely that, anti-inflammatory and antagonizing effects of Th-2 cytokine-mediated down-regulation on the Th-1 cytokines improves psoriasis during pregnancy[88].

ASSOCIATION OF PSORIASIS AND AUTOIMMUNE DISEASES:

We reviewed studies published in the MEDLINE database from January 1, 1980, to June 1, 2011, and recapitulated the associations between psoriasis and several key autoimmune diseases, including celiac disease (CD), inflammatory bowel disease (IBD), multiple sclerosis (MS), systemic lupus erythematosus (SLE), and autoimmune thyroid disease. This review shows that the association among psoriasis and CD and IBD appears to be well described[98].

ANEMIA IN PSORIASIS:

Psoriasis is known to be one of the skin diseases which can cause folate deficiency. Touraine et al[101] reported reduced serum and red blood cell folate levels in 22 out of 50 patients with psoriasis. Similar observations have also been reported by Shuster and Marks and Fry et al. They attributed the folate deficiency mainly to the increased utilization of folate by the rapid turnover of epidermal cells in psoriasis. The malabsorption of folate first proposed to occur in psoriasis by Shuster and Marks has since been noted only in rare cases by Touraine et al. Folate deficiency due to excessive loss in exfoliated skin was suggested by Hild, but was ruled out by Fry et al. In

contrast to the reduced folate levels, serum vitamin B12 levels are reported to be normal in most psoriasis patients and no evidence of impaired vitamin B12 absorption has been detected despite abnormal Schilling test results in some cases. In addition, there is no increased incidence of pernicious anemia in psoriasis patients to our knowledge. These findings suggest that vitamin B12 deficiency is unlikely to be a contributory factor in the megaloblastic anemia in psoriasis[99].

C-REACTIVE PROTEIN:

In 1939**,** Tillet and Francis described material in the sera of acutely ill patients. It was attached to the cell wall C-Polysaccharide of Streptococcus pneumonia and agglutinated the organisms. In 1941 that material was revealed to be a protein and called as C - reactive protein.

Evolution of CRP and pentraxin:

It belongs to pentraxin family of calcium dependent ligand binding plasma protein. The pentraxin family, is vastly conserved in evolution. It is called for due to its electron microscopic appearance and from the Greek penta(five) ragos(berries) with homologous proteins throughout the vertebrates and even in phylogenetically distant arachnid, limulus polyphemus, a horseshoe crab[71].

In spite of the evolutionary preservation of sequence, protein fold and subunit organization there are notable deviation between CRPs of different species.

The disparities are based on with regard to

- Presence and character of glycosylation,
- capability to precipitate and aggregate ligands
- Fine ligand-binding specificity,
- Protomer assembly
- Behavior as acute-phase proteins
- Base line circulating concentrations
- Capacity to activate autologous complement.

Indeed, only human CRP has been meticulously known to activate complement in isologues serum. These differences dominate in extrapolating from animal models to humans[71].

Synthesis:

In the hepatocytes it is synthesized, nearly exclusively a large amount under the control of cytokines. But extra hepatic sites of CRP production have also been reported [69].

IL-1, IL-6 and TNF-α mostly controls the synthesis of CRP. These cytokines has power to alter the CRP levels as well and increase of CRP in blood and body fluids by a steady release of these proinflammatory cytokines[79].

Biochemistry of CRP:

CRP is made up of five identical, non glycosylated polypeptide subunits each MW of 23,028 Dalton. All are non covalently attached to form a annular

or disk configuration by way of radial symmetry. The total mass of CRP is ~ 115kDa. Every subunit having 206 aminoacids.

The family name pentraxin for CRP has come because of its pentameric structure. Other related proteins to CRP, belongs to pentraxin family are proteins such as serum amyloid-P and pentraxin-3.

CRP has circulating half life of 18-20 hours[70,71]. Each protomer has the characteristic "lectin fold", composed of 2 layered β-sheets with flattened jellyroll topology. The ligand-binding site, composed of loops with two calcium ions bound 4 Å apart by protein-side chains, is located on the concave face. The other face carries a single α helix[71].

Function of CRP:

- Against break down products of cells and infectious organisms it has non specific host defense.
- Stimulate the classical complement pathway by starts at C1q, resulting in paghocytosis via C3b receptors.
- Has positive feedback via alternative pathway by make a complex with factor H, a complementary inhibitory factor and to a great extent reduces the activation of late components(C5- C9).

No genetic abnormalities have been reported for circulating CRP. It is catabolized when complexes are engulfed by phagocytes.

Reference interval of CRP:

In adults $\leq$ 5 mg/L.

Clinical significance of CRP:

The synthesis rate is the only determinant of circulating levels of CRP because the plasma half-life of CRP is stable in all conditions of health and disease. Thus the rate of synthesis is directly proportional to the intensity of pathological process inducing the CRP production[72].

It is one among the strongest acute phase reactants [69]. The plasma levels can rise up to 1000 fold after stress, trauma, myocardial infarction, infection or neoplastic proliferation. In the infection and inflammatory conditions it may go up to more than 5 to 10 mg/L. Only in moderate and severe forms of disease might have the high CRP level inferred from the literature and there is no enough data signifying a similar connection for mild disease.

Moreover, CRP may serve interchangeably with Psoriasis Area and Severity Index (PASI) as a measure of disease severity in the case of untreated psoriatic patients who do not have disease related arthritis[56].

Role of CRP in psoriasis:

It is recognized as the most sensitive indicator of inflammation, even though it is a nonspecific cytokine. Depends amount of tissue injury and inflammation severity, the magnitude of CRP level will be increased.[72].

When compare the Psoriatic patients with severity of the disease the severe forms (PASI > 10) had appreciably elevated levels of CRP than with mild disease (PASI < 10) (44% vs 25%) (*P* value = 0.003). Thus, these results

show the characterization of CRP level in psoriasis. That is as an inflammatory response that worsens with increasing disease severity. Several other studies have also reported a correlation between PASI and increased levels of CRP. Thus, CRP can be considered as a useful marker of disease severity. And can be used to observe the disease course and severity and can able to decide the treatment[68].

CRP estimation is widely available, inexpensive, and can be simply carried out in an outpatient clinical setting. To evaluate psoriasis disease severity, CRP along with PASI can be used as a powerful and sensitive marker, when it is difficult to evaluate, based on visual evaluation of the lesions. It can be used for screening of the disease course and treatment. Elevation of CRP may be thought as a risk factor for CVD in psoriatic patients because there is some research supporting the association between inflammation and CVD in psoriatic cases[68].

CLASSIFICATION OF PSORIASIS:

I. **Depends on natural history or morphology. (clinical appearance)**
II. **Depends on the precipitants or age.**
III. **Depends on the involved specific sites.**

I. Depends on natural history or morphology: (clinical appearance)

a. Plaque psoriasis (psoriasis vulgaris)

b. Acute guttate psoriasis

c. Unstable

d. Erythrodermic

e. Pustular

f. Inverse

II. Depends on the environmental factors:

a. Photo aggravated

b. Drug induced or exacerbated

c. HIV-induced or exacerbated

d. Alcohol misuse

e. Cigarette smoking.

f. Trauma

g. Metabolic factors

III. Depends on the involved specific sites:

a. Scalp

b. Flexural (inverse)

c. Genital

d. Nonpustular palmoplantar

e. Nail

f. Mucosal

g. Ocular

h. Facial

I. Depends on natural history or morphology: (clinical appearance)

a. Plaque psoriasis: (psoriasis vulgaris)

This is the most common type of psoriasis. In this type, there is a stable; red (salmon pink) scaly lesion with gradual broadening of plaques lesions persists for months to years. They expand very steadily and progress as indolent course and rarely occurs abruptly. The scaling extension may differ and orange-brown or waxy yellow. The most commonly involved areas are the elbows, knees, gluteal cleft and the scalp. There is a symmetrical involvement in the affected areas[65]. The clear marginal zone, called the halo ring of Woronoff may enclose the lesion.

b. Guttate psoriasis: (eruptive psoriasis)

Most frequent in children and young adults. It arises in persons with no psoriasis or in people with chronic plaque psoriasis. Patients present with shower of tiny 2 to 3 mm erythematous, scaling papules, mostly follow the upper respiratory tract infection due to β-hemolytic streptococci. Pityriasis rosea and secondary syphilis are the differential diagnosis for the guttate type[65,76]. Mainly affected sites are the trunk, face, and proximal portions of limbs. Guttate psoriasis also detected after withdrawal of corticosteroid therapy and sunburn. Prognosis is best for children with limited disease [66.]

c. Unstable psoriasis:

This term usually explain the stages of disease, which is highly active and with unpredictable outcome[76]**.** Patients have frequent complaints of more itchiness, irritation and even pain**.** They are more intense inflammation with angry looking lesions. These seem to be ill demarcated, mild scaling and more red in color with intermittent exudation and crust. Further spontaneous conversion to pustular or erythrodermic psoriasis can happen. Inappropriate use of corticosteroids, excessive irritation, sunburn are some of the reasons usually associated with unstable psoriasis[25,57]

d. Erythrodermic psoriasis:

When affects around 90% of the body surface as a generalized form, it is described as erythrodermic psoriasis. Although the affected patient is having all the symptoms of the disease, but the generalized erythema is the most outstanding feature with less scaling. The face is rarely involved. It may present as different stages as sudden appearance of generalized erythema or gradual evolving from chronic plaque psoriasis. Triggering causes are occasionally identified[25,57].

e. Pustular psoriasis:

Numerous tiny pustules develop an erythematous skin with pustular plaques and inconsistent scale. This type of psoriasis is either mild and localized in soles and palms, or extensive and life threatening [64]. Localized mild form is easily baffled with eczema. But generalized form, coupled with

fever for a number of days, , diffuse cutaneous and mucosal pustules with a background of severe erythema, leukocytosis, arthralgia, secondary infection and electrolyte disturbances[64,65] episodes of fever and pustules are recurrent.[65] A severe, acute form (the von Zumbusch variant) can cause life-threatening complications.

f. Inverse psoriasis:

Affect the intertriginous areas including the axilla, groin, submammary region and naval. It also affects scalp, palms and soles. The individual lesions are finely demarcated plaques, with absence of scales because of their presenting areas and they may be moist[65].

II. Depends on the environmental factors:

a. Photoaggravated:

Usually the sunlight is favorable, but in little insignificant number of patients, psoriasis is aggravated by strong sunlight and it is the reason for summer exacerbations in exposed skin. Recent work has indicated that severely photosensitive psoriasis is predominantly female, strongly associated with onset age, HLA-Cw6 and family history, and different from polymorphic light eruption (PLE). Photochemotherapy (PUVA) may be useful in these patients.[76]

b. Drug induced or exacerbated:

In current clinical practice, the generally common drugs which may be worsen the psoriasis are Beta-adrenergic blocking agents, Lithium salts, Non-

steroidal anti-inflammatory agents, Synthetic antimalarials, Angiotensin converting enzyme inhibitors, and withdrawal of Corticosteroids[76,67].

Action of some medications is partially described. Such as, lithium salts raise proinflammatory cytokines, and rousing the cutaneous leukocyte recruitment; beta-adrenergic blockers may provoke epidermal hyperproliferation along with a decline of intraepidermal cyclic AMP; and chloroquine impedes epidermal transglutaminase, an enzyme that is crucially involved in the terminal differentiation of keratinocytes[91].

Both tachyphylaxis and rebound phenomenon can occur, even though the psoriasis may be retort to oral corticosteroids. Withdrawal of corticosteroids may lead to development of unstable psoriasis or rebound the disease and, so the withdrawal should be secured by stable dose reduction rather than sudden termination[67].

c. HIV and psoriasis:

HIV infection is one of the important triggering factors. [67].The initial clinical manifestation may be psoriasiform dermatitis. There are two different clinical patterns either guttate pattern with large plaques or diffuse psoriasiform dermatitis [91].

AIDS sometimes may aggravate psoriasis, in which the helper T cell is he major target. The proof is the improvement of psoriasis with the treatment of cyclosporine, which hampers the helper T cell function, creates a paradox that remains to be fully explained[76].

d. Alcohol misuse:

Excessive alcohol consumption is associated with moderate to severe psoriasis [67]. Alcohol may not seem to be to induce psoriasis but worsens the preexisting disease. This effect seems greater in men when compare with women. Heavy drinkers tend to have more extensive and inflamed disease. Abstinence has been turned up to encourage remission [76,77.]

e. Cigarette smoking:

There is a predominantly a well-built association between palmoplantar psoriasis and cigarette smoking. Smokers are at greater risk of getting psoriasis, and more prone to suffer with severe disease and having psoriatic arthritis[76].

Smoking provokes morphologic and functional alterations in polymorphonuclear leukocytes, which causes an overstated discharge of chemotactic factors. In some studies have shown that cigarette smoking causes an overproduction of transforming growth factor β, tumor necrosis factor α and interleukin 1β, which have been coupled with psoriasis severity[92].

f. Trauma:

A vast array of local injurious stimuli has been recognized to sketch psoriatic lesions, includes chemical, physical, infective and inflammatory and surgical insults[76].

Psoriasis in which, the different types of trauma may elicit the disease in previously uninvolved skin, is called Koebner phenomena. The reported

incidence of Koebner reaction has a wide-ranging between 38- 76% and it occurs usually after 7-14 of injury[76,57,64].

g. Metabolic factors:

The early onset of psoriasis in women, with the peak around puberty, changes around pregnancy and provocation of psoriasis by high dose estrogen therapy would-be indicate a role for hormonal influence in disease[76].

III. Depends on involved specific sites:

In Psoriasis the skin of elbows, knees, scalp, lumbosacral region, intergluteal cleft and glans penis are the regions affected habitually[64].

a. Scalp:

One of the commonest regions to be first affected in psoriasis is scalp. And it is the chiefly affected area in plaque psoriasis. Plaques have a tendency to be limited to hair-bearing areas, mainly at the occiput. Extends a short distance away from the hairline around the ears. The hair growth rate is normal. Sometimes severe hair loss is associated with psoriatic erythroderma. A morphological entity includes the plaques firmly adherent to the scalp and related hair, asbestos-like scaling, has been termed as pityriasis amiantacea. It is most common in young children and adult.

b. Flexural psoriasis: (Inverse psoriasis)

Affecting the inguinal creases, axillae, submammary folds, gluteal cleft, umbilicus, and other body folds. More common in older adults and obesity. Often seen with plaque psoriasis. May occur as primary disorder or Koebner

phenomenon on top of infective or seborrheic intertriginous dermatoses. Sometimes it arouses suspicion of failure to react to antibacterial and antifungaldrugs.

Fissuring at the depth of the crease and a glassy hue on the lesional surface is commonly seen. Usually well-defined edges seen around the lesion, except secondary infection or medicament dermatitis.

c. Genital psoriasis:

Can be considered as a type of flexural skin and there are similarities between psoriasis as it affects flexural and genital sites. The occurrence of genital involvement is to be low, but this area is not much mixed up along with other areas.

d. Palms and Soles:

Present as a characteristically scaly areas with a fine silvery scale over the lesion. It can be stimulated by scratching. Psoriasis keeps hold of its typical character, elsewhere on the hands and feet. There may be association between lesions and occupational irritants or trauma.

e. Nail:

Common in psoriasis patients with concurrent PSa, incidence around 70% patients. All types of psoriasis of the skin associated with nail involvement mostly. There is no sex predilection. When compare with those under the age of 20 years, patient over 40 years of age are affected twice[76].

The most common findings are observed are pitting, dimpling, subungual hyperkeratosis, yellow brown(often likened to an oil slick) discoloration, ridging and thickening & crumbling of nail plate separation of the nail plate from underlying bed(onycholysis)[54,55,64].

f. Mucosal lesions:

True mucosal involvement appears to be rare. But the plaque, erythrodermic and pustular forms associated with mucosal involvement. Geographic tongue and association of psoriasis with HLA-Cw6 provides further evidence that the two disorders are related.

g. Ocular lesions:

Ocular involvement is either directly, or by associated immunological phenomena. The most frequent ocular complications of psoriasis involvement of the eyelids or eyelid margins can leads to blepharitis. Xerosis and chronic non specific conjunctivitis is also seen in psoriasis. Keratitis is rare. Uveitis is observed with extensive psoriasis and an immunologically interceded complication.

h. Facial psoriasis:

It is the marker of severe psoriasis. Involvement of face occurs in patients with long duration of the disease or early onset or with nail or joint involvement often involved with face. More extensive treatments is needed for this patients. Positive family history, more severe pruritus, , and history of Koebner response are associated with facial involvement[95].

IMPROVING THE QUALITY OF CARE:

Physician Global Assessment:

In psoriasis, the PGA scoring system is build on response to treatment as measured by lesion erythema, induration, and scale, with score assignments that range from clear, almost clear, mild, moderate, to severe. The PGA system demonstrates has both substantial correlation and reliability, when compared with the other widely used assessment tool like the Psoriasis Area and Severity Index. PGA scale that has undergone psychometric validation and found to have internal consistency, strong test-retest reliability, and validity on top of significant longitudinal correlation to the Patient Global Assessment (PtGA)[97].

Table 6: PGA grading scale: (contain a 5-point range from clear to severe)[97]

SCORE	DEFINITIONS	DESCRIPTION
0	Clear	No signs of psoriasis. But postinflammatory discoloration may be present.
1	Almost clear	Only minimal plaque elevation, scaling and erythema
2	Mild	Easy recognizable. Less than half of the face involved.
3	Moderate	Moderate plaque elevation. Scaling and erythema.
4	Severe	Very marked plaque elevation. Scaling and erythema

PRINCIPLES IN MANAGEMENT OF PSORIASIS[78]:

Concentration of the care of psoriatic patients involves superfluous treatment for the skin lesions and arthritis. Difficulty in psoriasis is, only recommend the drugs alone not sufficient in manage the disease but the required care is an unexpurgated complete individual approach of health care.

Psoriasis management takes account of uncover the related comorbidities like cardiovascular disorders, hypertension and diabetes mellitus, dyslipidemia. More over psoriasis patients have more chances to undergo depression and nervousness and strong idea of suicide.

At standard interval the screening for the following,

- The other related disorders
- Drug-triggered psoriasis
- To avoid drug-drug interactions prescribe co-medication
- Recognition of trigger factors and their treatment

Understanding triggers:

So many causative factors are documented as a reason for early symptoms of psoriasis to flare up of stable long term psoriasis. Realizing and lessening of these stimulating factors is an essential component to deal with psoriasis.

- Based on different researches from various countries, obesity is identified as a noteworthy trigger for psoriasis. These patients show improvement in

skin lesions with undergoing bariatric surgery with subsequent significant weight loss. Obesity is also related with reduced efficacy of psoriasis treatment and itself is an self-sufficient risk factor for cardiovascular disease. Thus, can add the weight loss intervention programs as a part of psoriasis management.

- Tobacco smoking is one of the most important risk factor. Counseling of cessation of smoking cessation ought to be engaged in care giving.
- Some infections are being capable of act as cause for psoriasis, for example streptococcal throat infection is one of the main exaggerating factors. Recurrent tonsillitis in grown persons with psoriasis, tonsillectomy can lessen the symptoms of psoriasis and minimize the requirement for treatment. Periodontitis has also known to be a risk factor of psoriasis.
- Apart from of the stressor's nature, stress is a significant a strong aggravating factor in all age groups.

TREATING THE SKIN MANIFESTATIONS:

Three main types of therapy[57,78]:

A. topical therapy

B. Phototherapy

C. Systemic therapy

1. Mild psoriasis:

Topical therapy is usually used to treat mild cases, but reaction to therapy in not satisfied, proceeds phototherapy. PUVA is used to treat and its efficacy is extensively documented and confirmed by various studies.

2. Moderate to severe psoriasis:

Require systemic therapy. Methotrexate, cyclosporin, acitretin and Etretinate are usually used as first-line medications. Biologic agents and fumaric acid esters are can be offered as a systemic therapy. Other than retinoids, all therapies for psoriasis are primarily anti-inflammatory to slow down keratinocyte proliferation and suppress the severity of plaques.

In the therapeutic armamentarium for patients with moderate-to-severe psoriasis and psoriatic arthritis, the biologic agents are the better option. Patients must be scrupulously monitored to assess the patients whether they can tolerate the biologic therapy because of potential side effects. This screen should include close attention to the patient's past medical history as well as baseline laboratory testing.[87]

Table 7: Psoriasis treatment options on the WHO model list of essential medicine:

a) Anti-pruritic and anti-inflammatory medicine:

Hydrocortisone	Cream or ointment 1% (as valerate)
Betamethasone	Cream or ointment 0.1% (acetate)

b) Drugs lessen skin proliferation and demarcation:

Salicylic acid	Solution 5%
Urea	Ointment or cream 5% or 10%
Coal tar	Solution 5%
Flurouracil	Ointment 5%

c) Systemic therapy:

Cyclsporine	Capsule 25mg (for immunosuppression)
Methotrexate	Tablet 2.5mg (as sodium salt) (for joint disease)

As per Sofen H et al study in 2014, in their double blind, randomized, placebo-controlled study of the tolerability, safety, and clinical effect of an anti-IL-23-specific mAb, guselkumab was assessed in patients with moderate-to-severe plaque psoriasis. The clinical response of the moderate-to-severe psoriasis to IL-23 inhibition with a single dose of guselkumab results, suggesting that neutralization of IL-23 alone is a promising therapy for psoriasis[106].

BARRIERS IN QUALITY CARE: [78]

- **Inadequate awareness of health professionals**

Lack of awareness of psoriasis is mostly due to inadequate instruction to general physicians and other health-care contributors. Contact with specialists at the needed situation is to make certain favorable treatment and avoidance of associated disorders.

- **Limited access to health care:**

Fundamental problem met by patients. The deficit in adequate access to health professionals and insufficient number of professionals contributes low

public awareness of psoriasis and without diagnosis, without treatment, uninhibited progression in disease severity and disability

- **Lack of guidelines and tools for treatment**

Have consequences like uncontrolled disease and redundant suffering, irrevocable joint deformities and disability. Individual comprehensive personalized care also often deprived. If health-care providers are conscious of guidelines and put into practice daily, the quality of care for psoriasis patients is increased.

- **Availability and cost of necessary drugs:**

Financing for treatment is disastrous to the patients and their family financial state of psoriatic patients. And also it is difficult to commence their work due to health conditions or because of bias.

- **Discrimination**

Discrimination in opposition to psoriatic patients is directly affecting the ability to proper health care access. A public misconception like it is a communicable disorder and ends up in omit the patients from the community and in day to day life by surrounding people leads to lack of self confidence and even promote the suicidal tendency among psoriatic patients.

- **Difficulties with adherence**

Patient adherence has inverse relationship with discontent in treatment and psychiatric morbidity. Reduced adherence is problem related to topical as well as systemic therapy which includes biologic agents, but highest with

topical therapy. It is to some extent due to lack in the communication regarding misperception of possible adverse events, directions on how to use the drug, and erroneous prospect about the speed and degree of deterioration of symptoms and signs.

KEY ACTIONS TO STRENGTHEN SERVICES:

- Developing better way to access the services and necessary medicines to control psoriasis.
- Organization of helpful procedures or steps that foster the development of organizations, offered support for psoriatic patients and their families.
- Ensuring the commitment of policy-makers and provision of adequate managerial support;
- Education and training for health care providers, particularly in primary care settings.
- Formation of an interior system among dermatologists and required pertinent specialists to available out on demand.
- Establishment of useful setups that promote the association establishment, which makes available help to psoriatic patients and families of them.
- Organization of health-education, counseling and self-care programmes for patients with psoriasis.

RELAPSE:

Eventhough with different modes of treatment, psoriasis is completely cured; there are more chances to have relapse. With 142 patients a follow up study of seven years duration was done. It shows that when compare with the home treated patients, there is a longer remission for the persons who got treatment in hospital whether outpatient or inpatient. Guttate lesions had the better prognosis[86,57].

EXPERIMENTAL APPROACHES:[57]

A fusion protein and diphtheria toxin as a intravenous therapy, anti CD-25 antibody, topical application of human recombinant IL-10 and oral macrolatums are some of the experimental and newer approaches .

MATERIALS AND METHODS

STUDY DESIGN : CASE CONTROL STUDY

PLACE OF STUDY : Department of Biochemistry and Dermatology, Govt. Kilpauk medical college, Chennai-10

DURATION OF STUDY : 6 months (MARCH 2016 – AUGUST 2016)

SAMPLE SIZE : 90

SAMPLE SELECTION:

CA11SES : 45 newly diagnosed cases of psoriasis

CONTROLS : 45 Nonpsoriatic healthy individuals with no Family history of psoriasis.

STUDY POPULATION:

INCLUSION CRITERIA:

- Newly diagnosed psoriatic patients in the age group of 21- 60 years.

The diagnosis of psoriasis was confirmed in all cases by dermatologist based on established clinical criteria.

EXCLUSION CRITERIA:

1) Psoriatic Patients on treatment.

2) Other type of skin diseases like atopic dermatitis.

3) Other inflammatory diseases like DM, HT, CAD, and BONE DISEASES.

4) Immunosuppression, Malignancies, Autoimmune/genetic/ metabolic/rheumatic diseases, and bacterial, viral, or fungal infection up to 4 weeks.

SAMPLE COLLECTION:

3ml of venous blood was drawn in a plain serum vacutainer tube under sterile conditions after fulfilling the selection criteria, from the anticubital vein with explicit informed consent. Keep the samples in a serum separator tube for 2 hours at room temperature to clot. Serum was separated by centrifugation at approximately 2000-3000rpm for 15-20min and aliquoted, into an eppendorf, and immediately frozen at -20°C and keeps it in storage until processed.

2ml of venous blood was drawn in EDTA tube for TC, DC.

ESTIMATION OF C-REACTIVE PROTEIN:

METHOD: Quantitative Turbidimetric Method.

Kit used: CRP-Turbilatex

Principle:

Latex particles coated with specific human anti-CRP are agglutinated when mixed with samples containing CRP. An absorbance change occurs due to agglutination which is, dependent upon the CRP contents of the patient

sample that can be quantified by comparison with a calibrator of known CRP concentration, in spectrophotometry at 540nm wavelength.

Reagent Composition:

Diluent (R1)	Tris buffer 20 mmol/L, pH 8.2. Preservative.
Latex (R2)	Latex particles coated with goat IgG anti-human CRP, pH 7.3. Preservative.
Calibrator (R3)	Liquid Calibrator. Human Serum. C-Reactive Protein concentration is stated on the vial label.

Reagent Preparation and Stability:

CRP Calibrator:

Reconstitute with1.0 ml of distilled water. Mix gently and incubate 10 minutes at room temperature before use. Once reconstituted is stable for 1 month at 2-8˚ C or -20˚ C.

Test procedure:

1. Bring the reagent and the photometer (cuvette holder) to 37C.
2. Assay conditions:
    - Wavelength ……540 nm
    - Temperature…….37˚C
    - Cuvette light path …… 1 cm
3. Adjust the instrument to zero with distilled water.
4. Pipette into cuvette.

Diluent R1	800 Ml
Latex R2	200 Ml
Calibrator or sample	5.0 µL

Mix and read the absorbance immediately (A_1) and after 2 minutes (A_2) of the sample addition.

Calculations:

$$\frac{\text{(A2-A1) sample}}{\text{(A2-A1) calibrator}} * \text{calibrator concentration} = \text{IU/ml CRP}$$

Reference value: Upto 6 mg/L

ESTIMATION OF INTERLEUKIN-23:

Method: Enzyme Linked Immuno Sorbent Assay

Kit used: sincere. Catalogue no: E13651016 (type II), 96T

Principle:

The kit assay IL-23 level in serum, use purified human IL-23 antibody to coat microtiter plate wells, make solid-phase antibody, then add samples to wells, combined human IL-23 antibody which with HRP labeled, become antibody-antigen-enzyme-antibody complex, after washing completely, add TMB substrate solution, TMB substrate become blue color, at HRP enzyme-catalyzed, reaction is terminated by the addition of a sulphuric acid solution and the color change(yellow) is measured spectrophotometrically at a wavelength of 450 nm. The concentrations of human IL-23 in the samples were determined by comparing the O.D of the samples to the standard curve.

Assay Procedure:

1) **Preparation of the Standard**:

- Set 10 Standard wells on the ELISA plates coated label①②③④⑤⑥⑦⑧⑨⑩.
- Add Standard 100μl to ①②, then add standard diluent 50μl to ①②, mix.
- Take out 100μl from①②, and then add it to ③④ separately, then add Standard diluent 50μl to ③④, mix.
- Then take out 50μl from③④, and discard.
- Then take out 50μl from③④ and add to⑤⑥, then add Standard diluent 50μl to the ⑤ ⑥, mix.
- take out 50μl from⑤⑥ and add to⑦⑧, then add Standard diluent 50μl to the⑦⑧, mix.
- take out 50μl from the ⑦⑧ and add to ⑨⑩, add Standard diluent 50μl to⑨⑩, mix.
- take out 50μl from⑨⑩ discard.

2) **Set wells separately**:

Set Blank well and Testing sample well. (Do not add sample and HRP-conjugate reagent into the blank comparison wells, other each step operation is same)

3) **Add Sample**:

Add Sample Diluent 40μl to testing sample well, and then add testing Sample 10μl (**Sample final dilution is 5-fold**). Then add Sample to the bottom

of Pre-coated well, do not touch the well wall as far as possible, and mix gently.

4) **Incubate**:

Incubate for 30 minute at 37° C after closing the plate with Closure plate membrane.

5) **Prepare the Washing Buffer:**

30-fold Wash Solution, diluted 30-fold with Distilled Water until 600ml and preserve.

6) **Washing:**

Uncover Closure plate membrane, discard liquid, dry by swing. Add Washing Buffer to each well, keep still for 30s then drain. Repeat this for 5 times, dry by pat.

7) **Add enzyme**:

Except the Blank well, add HRP-Conjugate Reagent 50μl to each well.

8) **Incubate**: Operation with 4).

9) **Washing**: Operation with 6).

10) **Color**:

Add TMB Chromogen Solution A 50ul and then add TMB Chromogen Solution B 50ul to each well, **evades the light** preservation for 15 min at 37˚C.

11) **Stop the Reaction**:

Add Stop Solution 50μl to each well, to stop the reaction (the blue color change to yellow color immediately).

12) Assay:

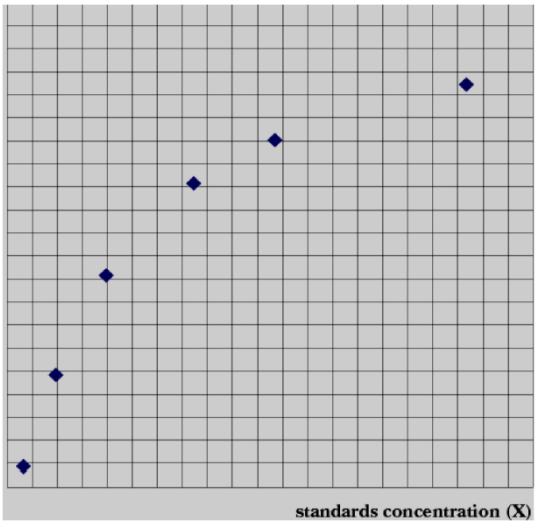
Set the OD of Blank well as zero, read absorbance at 450nm after adding Stop Solution **within 15min.**

- The judgment of result must take the OD of Microplate reader as a standard,

When use the dual-wavelength to assay, reference wavelength is 630nm.

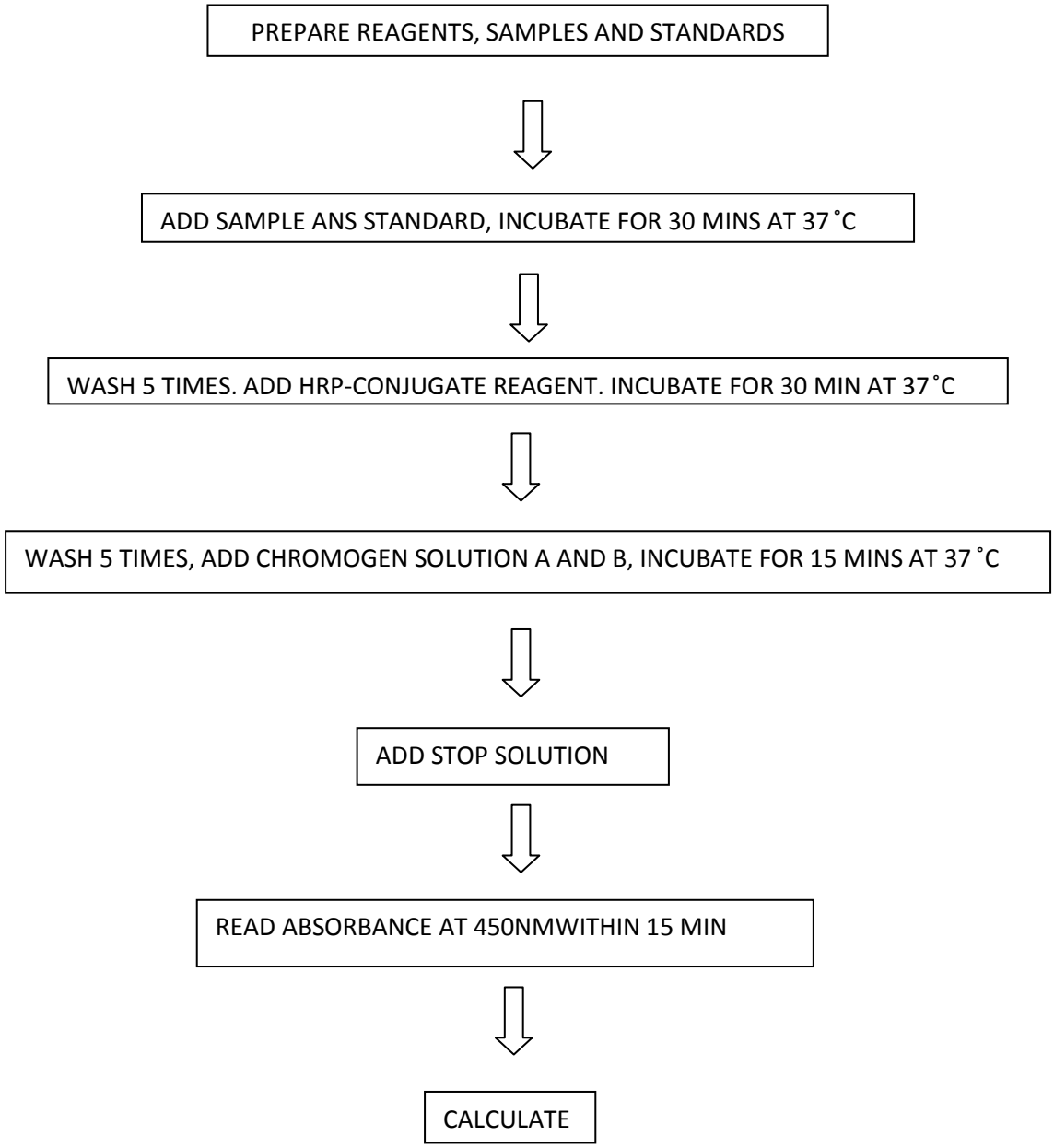
8. CALCULATE:

Take the standard density as a horizontal and the OD value on the vertical, obtain the Standard Curve, then find out the corresponding density according to the sample OD value, and multiplied by the dilution multiple **or** Calculate the straight line regression equation of the standard curve with the standard density and the OD value,with the sample OD value in the equation, calculate the sample density, multiplied by the dilution factor, the result is the sample actual density.



Note: This standard curve is provided for demonstration only. A standard curve should be generated for each set of samples assayed.

9. ASSAY PROCEDURE SUMMARY:



10. Performance characteristics:

This assay is designed to eliminate the interference by binding proteins, soluble receptors and other factors present in biological samples. No significant interference or cross reactivity between IL-23 and other cytokines.

Detection range: 7.6pg/ml – 500mg/ml

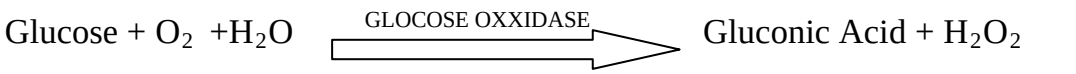
ESTIMATION OF GLUCOSE:

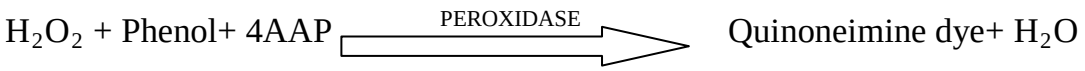
Method: glucose oxidase- peroxidase method. (GOD/POD) (END POINT METHOD)

Kit used: Erba.

Principle:

In serum glucose is oxidized to yield gluconic acid and hydrogen peroxide in the presence of glucose oxidase. The enzyme peroxidase catalyzes the oxidative coupling of 4-aminoantipyrine with phenol to yield a colored quinoneimine complex. The intensity of pink colored quinoneimine dye is proportionate to glucose concentration and was measured at 505nm.





Reagent composition:

Enzyme reagents and standard:

Ingredients	Concentrations
Glucose oxidase	≥ 20,000 U/L
Peroxidase	≥ 2,000 U/L
Phenol	10 mmol/L
Phosphate buffer	200 mmol/L
Glucose standard	100 mg/dl

Assay procedure: (Semi automated analyzer)

	Blank	Standard	Test
Sample	---	---	10µl
Standard	---	10µl	---
Enzyme reagent	1.0ml	1.0ml	1.0ml

Mix well after each addition and incubate at 37°C for5 minutes. And read the absorbance against 505nm.

Reference range:

Fasting: 60-100 mg/dl

Post prandial: 90-130 mg/dl

ESTIMATION OF BLOOD UREA

Method: UV - GLDH

KIT: Accucare

Principle:

The test is performed as a kinetic assay in which the initial rate of the reaction is linear for a limited period of time. Urea is hydrolysed by urease to NH_3 and CO_2. The NH_3 produced combines with alpha-oxoglutarate and NADH in the occurrence of glutamate dehydrogenase to produce glutamate and NAD.

$$\text{Urea} + H_2O \xrightarrow{\text{GLDH}} 2NH4 + CO2$$

$$NH_4^+ + \text{NADH} + H^+ + \text{2- oxoglutarate} \longrightarrow \text{Glutamate} + NAD^+$$

The initial rate of decrease in absorbance is directly proportional to the urea concentration in the sample. Absorbance is measured at 340nm.

Reagent composition:

Reagent I: buffer reagent

Reagent II: enzyme reagent

Urea standard: 50 mg/dl

Mix 4 parts (4 ml) of buffer reagent with one part (1 ml) of enzyme reagent and mix gently.

Assay Procedure :(Semi auto analyser)

	Blank	Standard	Test
Sample	---	---	10µl
Standard	---	10µl	---
Enzyme reagent	1.0ml	1.0ml	1.0ml

Mixed well and absorbance measured immediately at 340 nm.

Reference Range:

Serum/ plasma Urea → 15- 40 mg/dl

ESTIMATION OF SERUM CREATININE

METHOD : Jaffe's Method , Initial rate metho

Kit used : ERBA

Principle :

Creatinine in alkaline solution reacts with picrate to form a orange-yellow compound. The color is proportional to the concentration of creatinine in the sample when measured at 505nm.

Reagent composition:

Reagent I : Picric acid reagent.

Picric acid – 25.8 mmol/L

Reagent II: Sodium hydroxide reagent.

Sodium hydroxide – 95 mmol/L

Creatinine standard: 2 mg/dl

Reagents were allowed to attain room temperature. Equal volumes of reagent 1 and reagent 2 were mixed, waited for 15 minutes before use.

Procedure:

	Blank	Standard	Test
Sample	---	---	100µl
Standard	---	100µl	---
Enzyme reagent	1.0ml	1.0ml	1.0ml

To 1 ml of the reconstituted reagent 100µl of the plasma was added and absorbance (A1) taken at 20 seconds after mixing was noted & final absorbance (A2) at 80 seconds were measured.

Calculation:

A = A2 - A1

$$\text{Creatinine (mg/dl)} = \frac{\text{Absorbance of Test X concentration of standard (mg/dl)}}{\text{A of standard}}$$

Reference Range:

Males : 0.7 - 1.4 mg/dl

Females : 0.6 - 1.2mg/dl

TOTAL COUNT AND DIFFERENTIAL COUNT:

Method: Electrical impedance.

Instrument : Horiba Pentra

Model: ES60

Required sample:Micro-sampling from whole boold (CBC : 30 µL - DIFF: 53 µL)

Principle:

Whole blood is passed between two electrodes through an aperture so narrow that only one cell can pass through at a time. The impedance changes as a cell passes through. The change in impedance is proportional to cell volume, resulting in a cell count and measure of volume.

Reference range:

Total count	**4000- 10000 cells/cumm**
Polymorphs	**40- 75 %**
Eosinophils	**1-2 %**
Lymphocytes	**20- 45 %**
Monocytes	**2- 10%**
Basophils	**0-1%**

RESULTS

Table 1: Ratio of male/female among controls and cases

			Group		Total
			Control	Cases	
Sex	Male	Count	9	17	26
	Female	Count	36	28	64
Total		Count	45	45	90

There were no significant differences in male/female ratio between the patients and controls with p value 0.063. ($p > 0.05$)

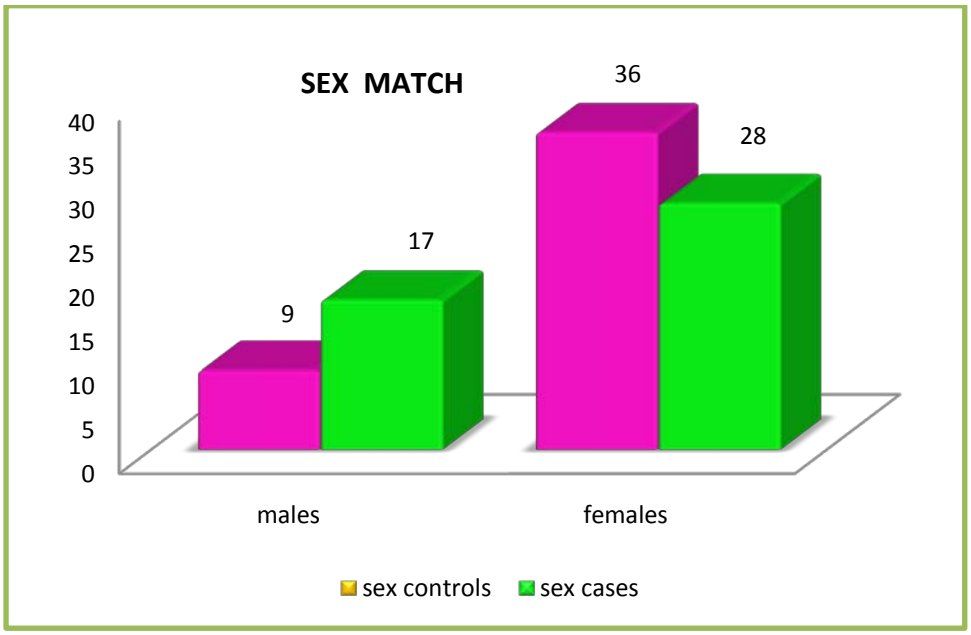
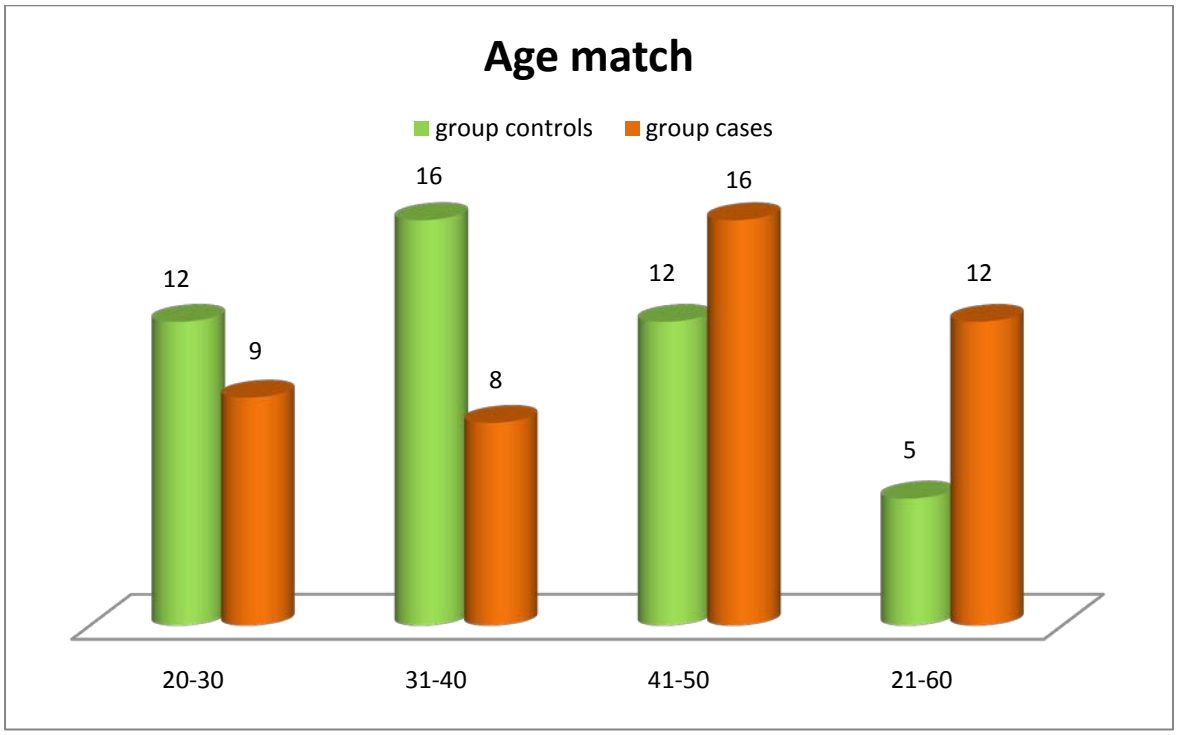


Table 2: Age match between cases and controls in study population

			Group		
			Control	Cases	Total
Age in years	20-30	Count	12	9	21
	31-40	Count	16	8	24
	41-50	Count	12	16	28
	51-60	Count	5	12	17
Total		Count	45	45	90

The age match between the cases and controls is insignificant. Here the p value is 0.088. That is > 0.05.



BLOOD, UREA AND CREATININE:

Table 3: Shows glucose, urea and creatinine values in between cases and controls.

Variables	Group	N	Mean	SD	p Value
Sugar	Control	45	137.40	66.22	0.563
	Cases	45	129.12	68.84	
UREA	Control	45	18.84	4.42	0.797
	Cases	45	19.15	6.79	
Creatinine	Control	45	0.87	0.19	0.214
	Cases	45	0.82	0.15	

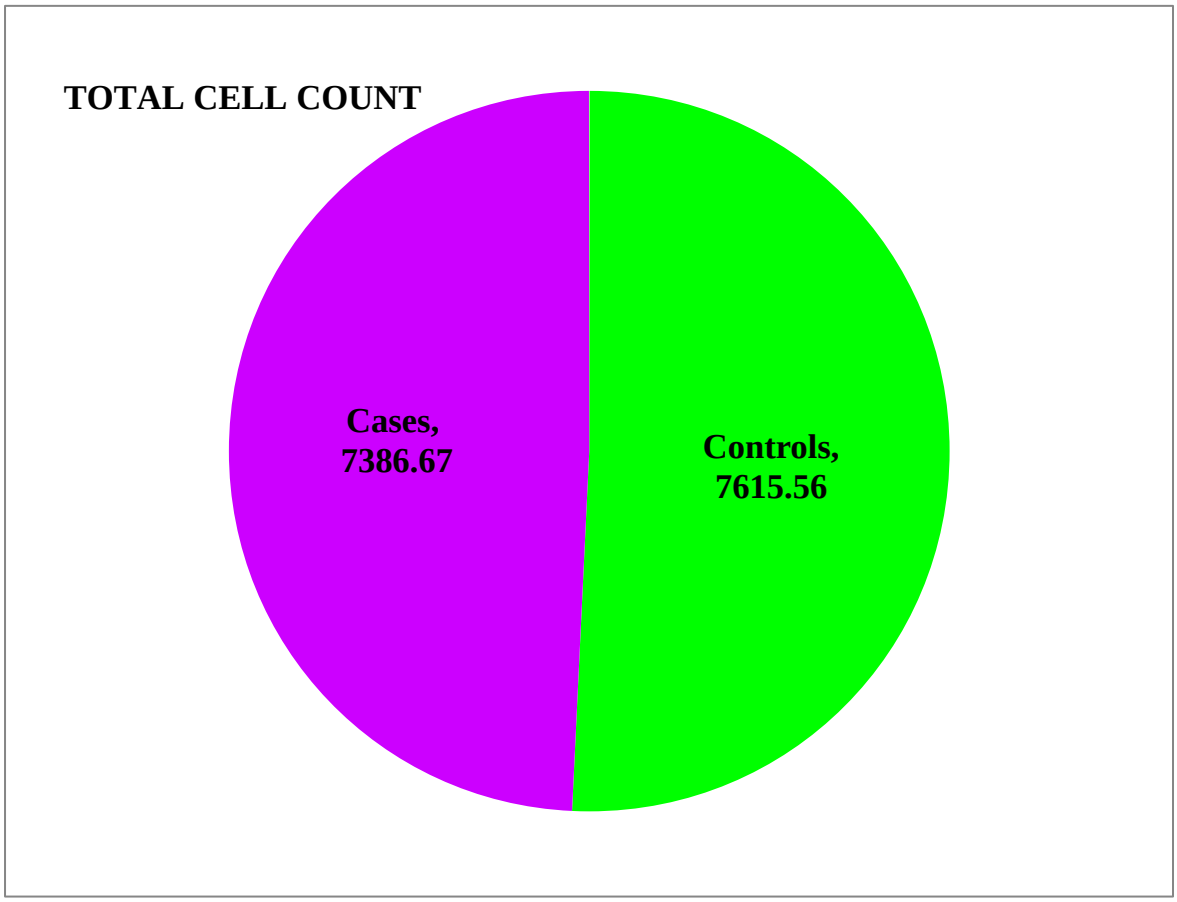
The table shows, the random blood sugar, creatinine and urea levels were within the normal range among the cases and controls. There is no significant difference between the controls and patients. (P> 0.05)

TOTAL COUNT:

Table 4: Shows the total count between controls and cases.

Variables	Group	N	Mean	SD	p Value
Total count	Control	45	7615.56	1860.34	0.537
	Cases	45	7386.67	1631.59	

The total count count between the patient and controls were not significant, with p value > 0.05 for al



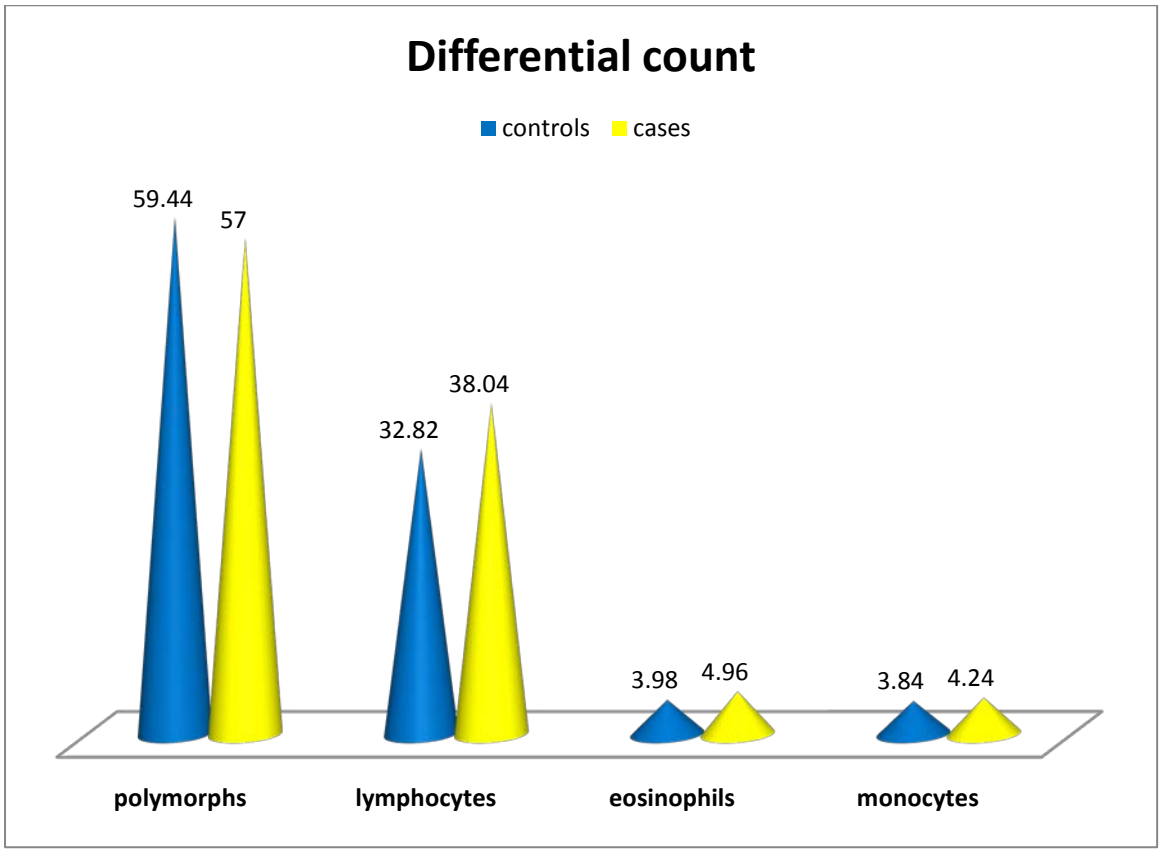
DIFFERENTIAL COUNT:

Table 5: Comparison of differential cell count between controls and cases

Variables	Group	N	Mean	SD	p Value
Polymorphs	Control	45	59.44	7.90	0.164
	Cases	45	57.00	8.59	
Lymphocytes	Control	45	32.82	6.66	0.265
	Cases	45	38.04	30.54	
Eosinophils	Control	45	3.98	3.81	0.203
	Cases	45	4.96	3.404	
Monocytes	Control	45	3.84	1.29	0.111
	Cases	45	4.24	1.04	

The differential count between the patient and controls were not significant, with p value > 0.05 for all. And the DC is within normal range in both controls and cases.

Comparison of differential cell count between controls and cases

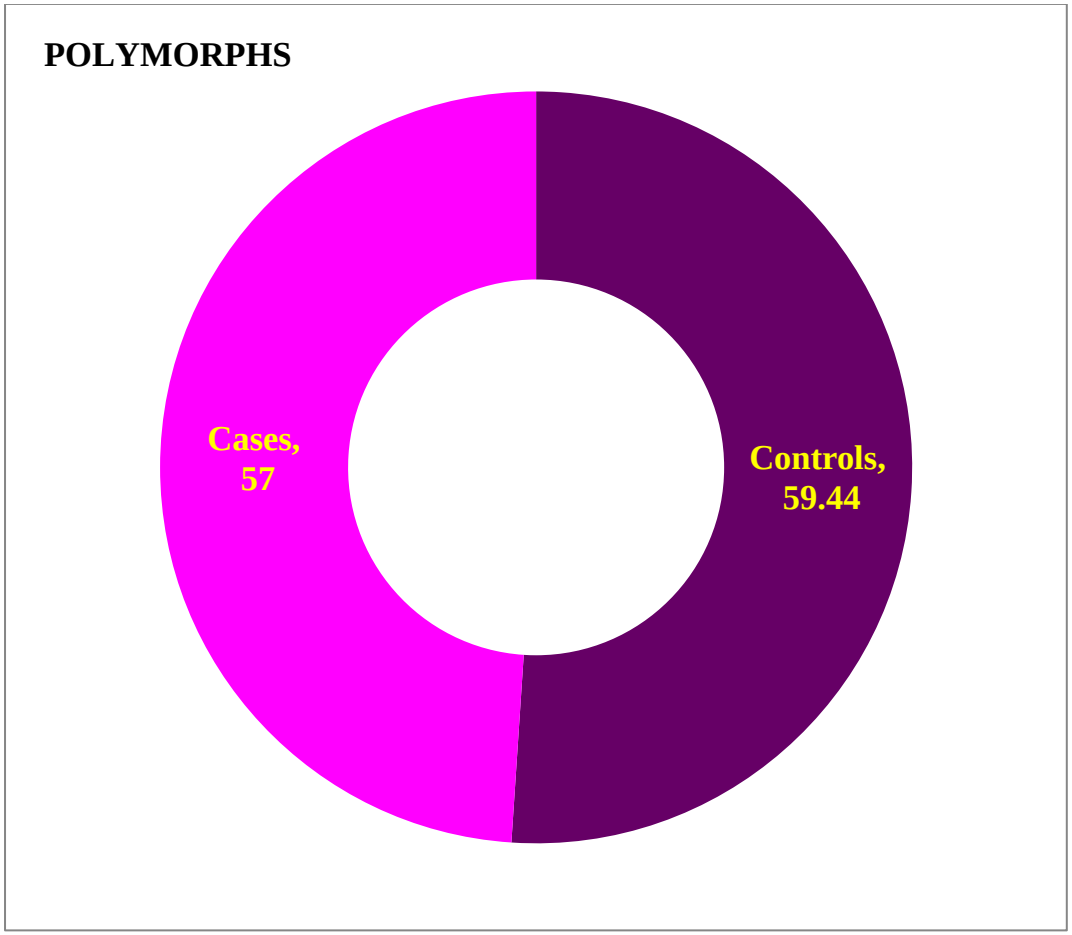


POLYMORPHS:

Table 6: Comparison of polymorphs among controls and cases

Variables	Group	N	Mean	SD	p value
Polymorphs	Control	45	59.44	7.90	0.164
	Cases	45	57.00	8.59	

The comparison between controls and cases in polymorphs shows the p value is >0.05 with non significant correlation.

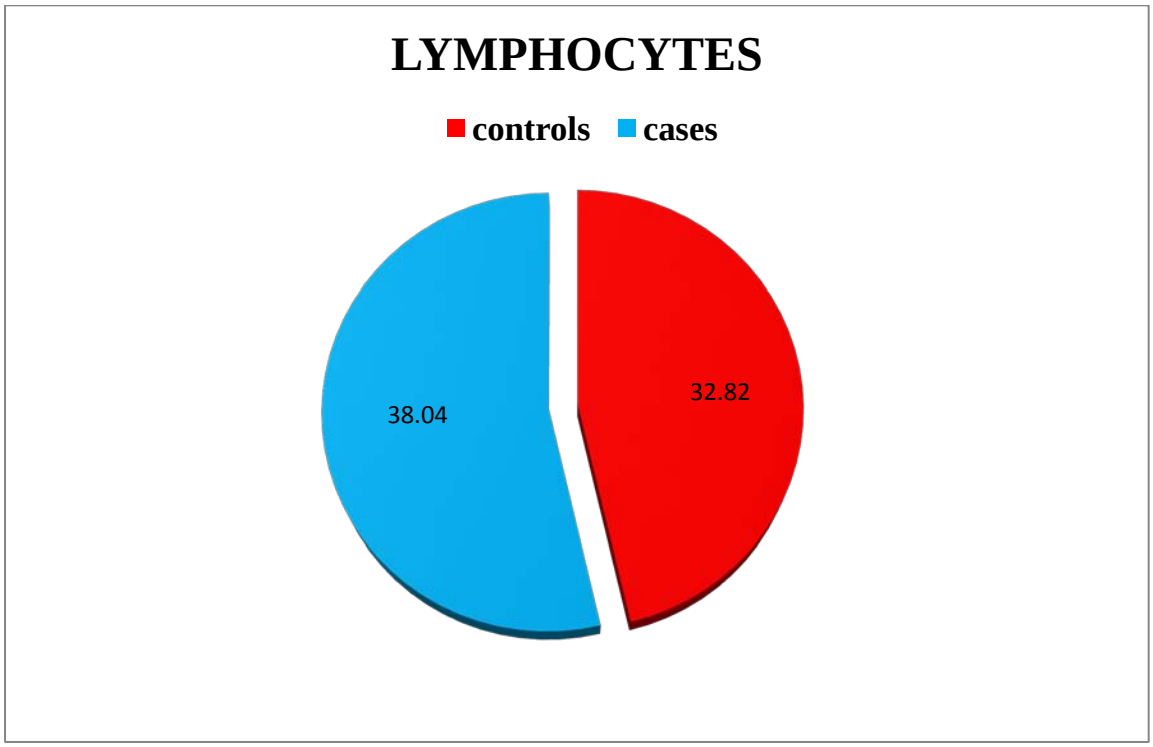


LYMPHOCYTES:

Table 7: Comparison of lymphocytes between controls and cases

Variables	Group	N	Mean	SD	p value
Lymphocytes	Control	45	32.82	6.66	0.265
	Cases	45	38.04	30.54	

The lymphocytes count among the study population shows the p value is > 0.05. It is insignificant.

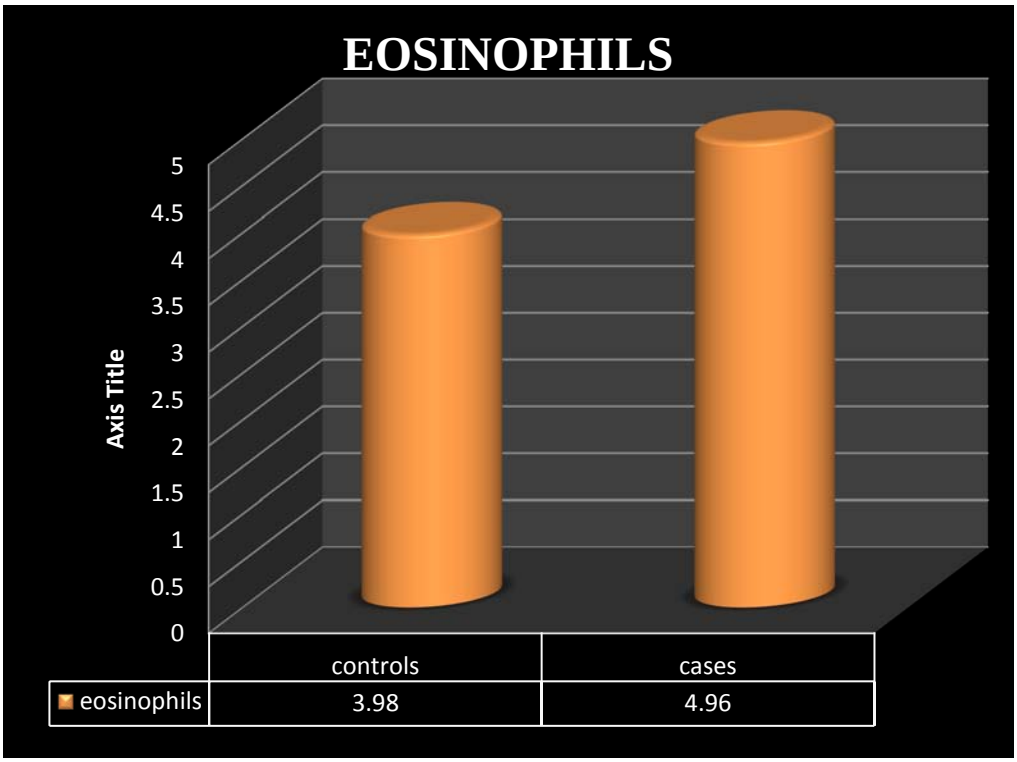


EOSINOPHILS :

Table 8: Mean comparison of eosinophils in controls and case.

Variables	Group	N	Mean	SD	p value
Eosinophils	Control	45	3.98	3.81	0.203
	Cases	45	4.96	3.404	

The P value is >0.05 for the eosinophils among controls and cases shows it is not significant.

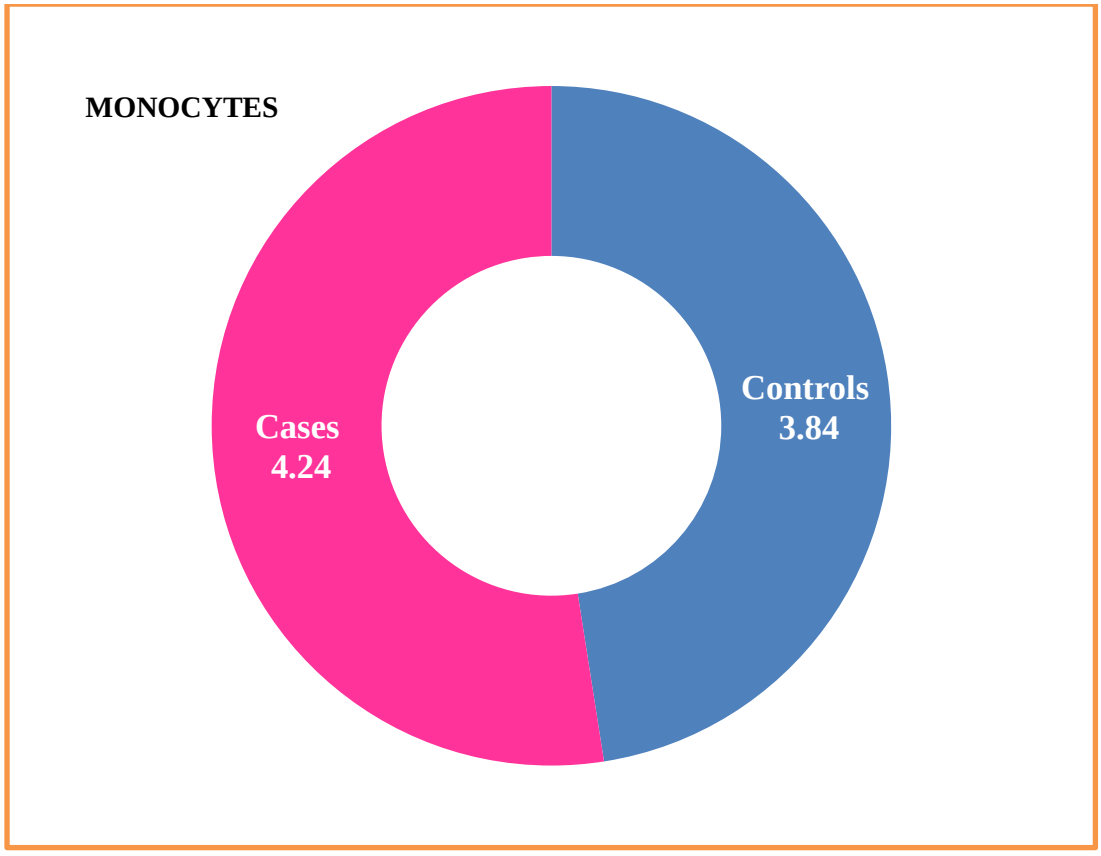


MONOCYTES :

Table 9: Mean comparison of monocytes among controls and case.

Variables	Group	N	Mean	SD	p value
Monocytes	Control	45	3.84	1.29	0.111
	Cases	45	4.24	1.04	

The P value is not significant for monocytes in the study population, because the P value is > 0.05.

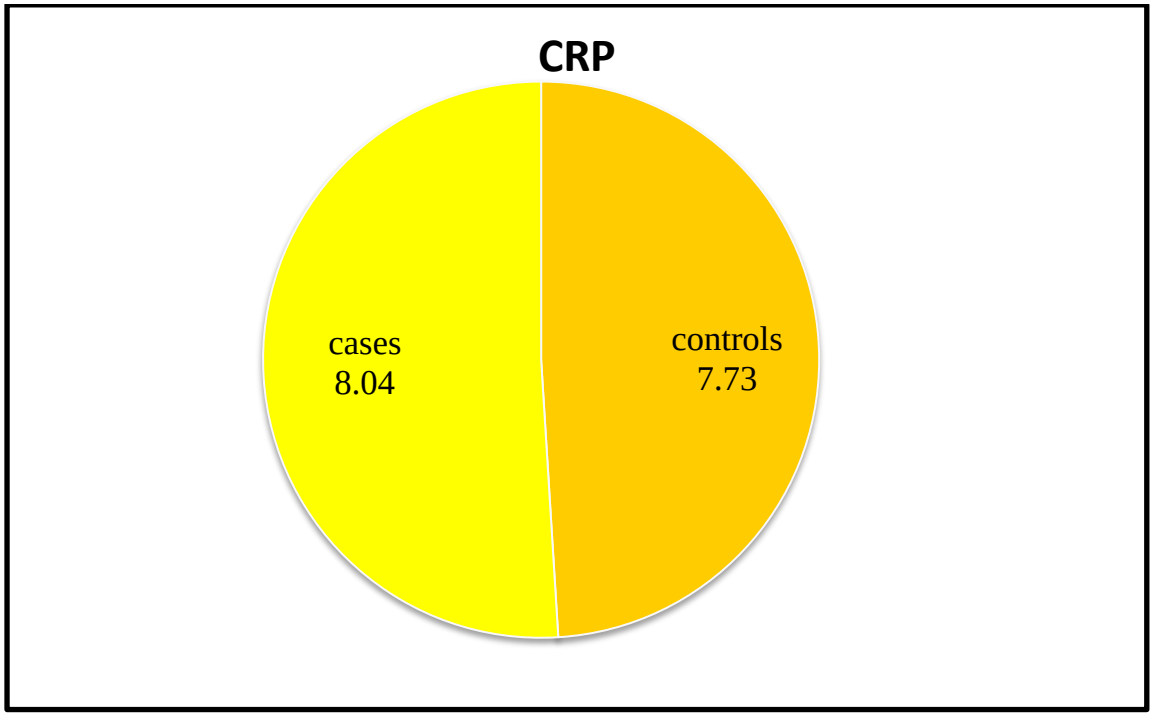


CRP:

Mean CRP was not significantly elevated in psoriatic patients when compared with controls (7.73 vs 8.04) .and statistically also not significant with P value 0.742

Table 10: Mean CRP among both cases and controls

Variables	Group	N	Mean	SD	p value
CRP	Control	45	7.73	4.27	0.742
	Cases	45	8.04	4.64	

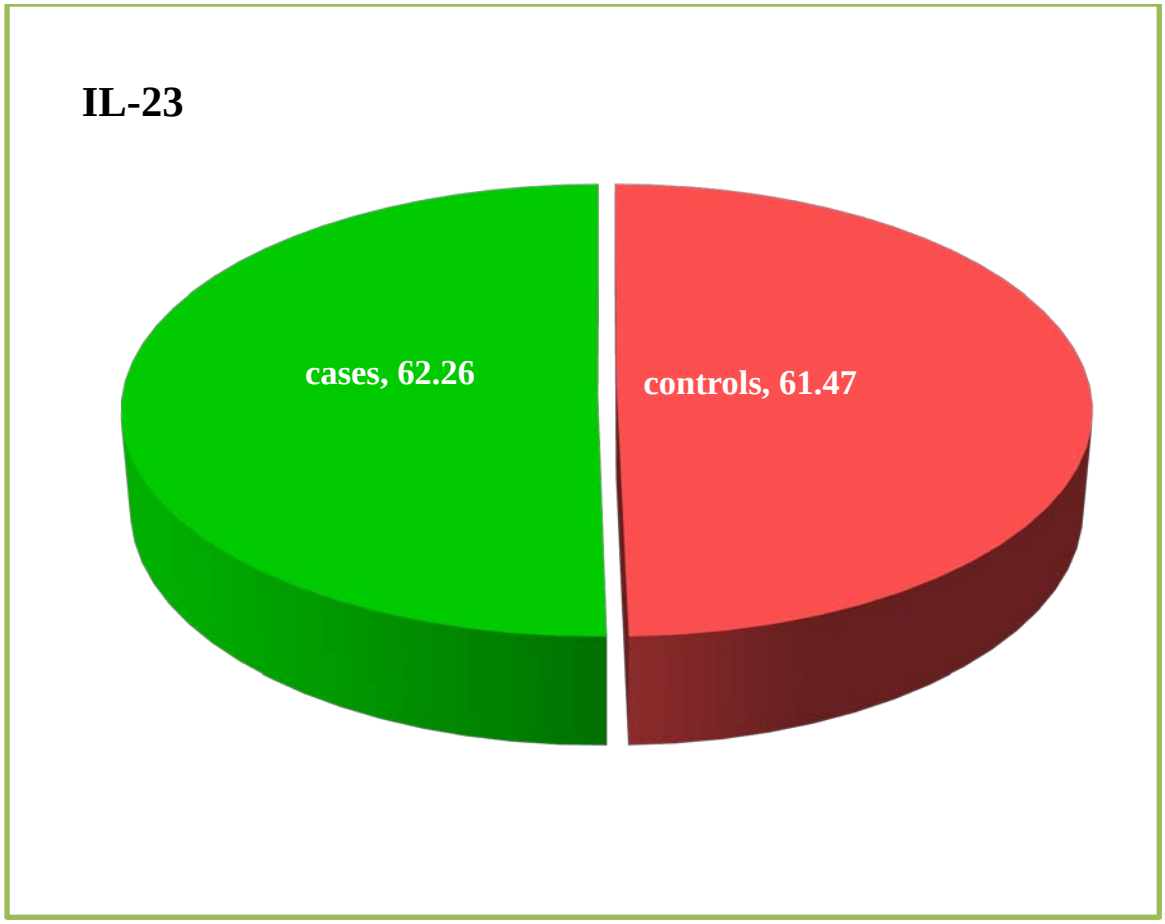


IL-23:

Table 11: Comparison between controls and cases.

Variables	Group	N	Mean	SD	p value
IL-23	Control	41	61.47	18.10	0.883
	Cases	45	62.26	29.74	

The mean value of controls and cases does not show any significant difference in the IL-23 titers. The P value is 0.898 which is > 0.05 clearly shows their significant relationship among the two groups.



DISCUSSION

The aim of my study is to estimate and assess whether IL-23 is a key tissue specific factor in pathogenesis of psoriasis and/or its functional capacity to act as a stimulating factor for the disease.

For the past 15 years from its discovery in 2000, IL-23 has promptly established as a key contributor and a probable therapeutic object in psoriasis than just a pro-inflammatory cytokine.[5]

Recently why IL-23 gets this much importance because, it is released in the early onset of disease and its level in serum is inversely related to disease duration as per Amina Hamed Alobaidi et al study[1].

It is suggested by Fotiadou C et al study in which, there is the possible crucial role of IL-23 and IL-17A in the early stages of the disease and activity of psoriasis [15].

Based on Sara Brenner study, therapies involved against the target IL-23 is showing early success in the treatment of plaque type psoriasis vulgaris[32].

As per Paola Di Meglio et al study, IL-23 was revealed has a major role in autoimmunity. In the past 3 years major advances in genetics, immunopathology and clinical findings of psoriasis, we can understand the fundamental role of the IL-23/Th17 axis [5].

Gretta L. Stritesky et al study supports the above statement that is; IL-23 sustains the population of IL-17 secreting T cells, noted as Th-17 cell

expansion or survival. Results of this study imply that IL-23 is a maintenance factor for the Th17 phenotype[27].

As per Anna Michalak-Stoma study, even though both IL-12 and IL-23 are present in psoriasis, IL-23, rather than IL-12, is vital during the pathogenesis of psoriasis. IL-23 is overexpressed in psoriatic skin, p35can be identified by, increased p19 and p40 mRNA levels but not always. IL-23 is overproduced by dermal keratinocytes, dentritic cells and in lesional psoriatic skin[30].

Based on above mentioned studies, I came to a thought that, the IL-23 has released from lesional keratinocyte and dentritic cells and maintain the population of TH-17 cells, which has a major role in pathogenesis of psoriasis.

In my study, I selected a total number of 45 patients (17 males, 28 females) and 45 age and sex-matched controls (9 males and 36 females) in population who attended the dermatology clinic first time with the features of psoriasis and normal persons from outpatient side in Government Kilpauk Medical College Hospital.

There were no significant differences in age among the controls and cases. The p value of sex match is 0.063, it is >0.05. The P value of Male/female ratio between the controls and patients is 0.088 and it is insignificant (P>0.05).

The selection of patients with psoriasis for my study was who are not undergone any previous local or systemic treatment. The patients were diagnosed clinically and selected for study as per dermatologist opinion. The

control group was included the healthy, nonpsoriatic volunteers with no family history of psoriasis.

Both patients and controls had a history, or clinically any findings or routine laboratory findings consist with, abnormal renal or function, or parasitic and any other infection.

The routine serum glucose, urea and creatinine estimation was done. The mean serum levels of blood sugar for controls was 137.40 mg/ml, while in psoriatic patients, it was 129.12 mg/ml. The difference was statistically not significant with p value 0.563(p>0. 05). The mean serum level of serum urea for control was 18.84 mg/dl. And for the cases it is 19.15 mg/dl with the difference between the two are statistically not significant with p value 0.797.The mean serum level of creatinine for controls was 0.87mg/dl and the cases 0.82 mg/dl with P value 0.214 (P >0.05) which is not significant statistically. So the serum sugar, urea and creatinine values are within the normal limits for cases and controls and statistically not significant implies that cases are not having any diseases which altered the above mentioned parameters.

The total and differential count levels were in normal range in patient and controls. The total count mean is slightly higher in cases when compare with controls. But both the groups, the counts are within the normal limits the p value is > 0.05, shows it is not a significant one. In differential count, the polymorphs mean value is slightly lower in cases than controls and the lymphocytes, monocytes and eosinophils values are slightly higher in cases.

But for all different cell types the p value is insignificant. So that's why in my study shows the lymphocytes values are slightly higher and neutrophils are having little bit low mean values. As per Peter J Aronson MD study, Neutrophils emerge very early in new psoriasis lesions. Neutrophils influences macrophage, Th1, Th2, and Th17 lymphocytes and their cell products including TGF-beta, IL-17, IL-22, and IL-23.The neutrophils count is low when compared to controls, otherwise within the normal limits.

As per E.J.Mundell et al study in 2011 in a survey in the US patients not receiving any treatment was almost 50% in the with mild psoriasis, 25% in the moderate psoriasis, and 10 percent of severe psoriasis[107]. Eventhough my aim is study in early cases of psoriasis, but the selected cases have comparatively high values of lymphocytes than neutrophils is may be the reason as per E.J.Mundell study.

The CRP level, comparison between both controls and cases, the p value is 0.742, which is not significant. The mean value of CRP level in control is 7.73 and for cases it is 8.04 and the p value is statistically not significant. Both controls and cases are having CRP level above the reference range that is above $\geq$ 6 mg/L. This has some reasons as per Aydin Nazmi et al article, low socioeconomic status is a risk factor for elevated CRP levels, even when several potential mediators of this association are controlled for. High levels of stress built up throughout the life, which is often mostly seen in the poor and disadvantaged, may adversely impact health outcomes and also have moderately high values of CRP. The overwhelming most of the articles in 32

studies reported, there is inverse associations between CRP levels and socioeconomic status and significant differences among racial/ethnic groups, even after controlling for possible confounding and mediating variables.[29] In my study population, the persons are attending the government hospital invariably they have been belongs to low socioeconomic groups.

The mean value of IL-23 level in controls it is 61.47 and for cases 62.26. In the mean value of controls and cases, there is only a little elevation in cases, but does not show any significance in p values. The p value is 0.898, which is > 0.05 clearly shows the non significant relationship among the two groups. These results of my study is may be due to the sample collection from government hospital, mostly they are belongs to low socioeconomic group. So there is an alteration in inflammatory markers range in controls also as per Annemarie Koster et al, their study analyzed the relationship between socioeconomic state and several markers of inflammation from a large sample of community-dwelling adults. The result is low socioeconomic status (SES) has been related to higher levels of inflammatory markers This is moreover, as inflammation is essence of a biological response of the immune system and it is associated with increased morbidity and mortality across the age span, including in old age.[34]

As per Michael Paalani et al study, Inflammatory based risk for health problems may vary according to ethnicity and other demographic factors. Exercise, diet and body mass like factors also show influence in the levels of inflammatory markers.[37].

As per Hideki Nakajima et al study no detectable serum levels of IL-23 was found in both the groups. There are possibilities that these cytokines may involve in the very primitive phase of psoriasis development or be present in the lesional skin only.[31]

As per Amina Hamed Alobaidi Serum levels of IL-23 highly significantly negatively correlated with disease duration[1].

In my study there is a nonsignificance between both controls and cases because of both the groups are belongs to low socioeconomic status as per Annemarie Koster et al or may be many patients are going without treatment due to unawareness of the disease as per E.J.Mundell et al [34],[107].

Further attempt should be mandatory in order to understand the inflammatory marker IL-23 in our community level and to execute observational studies in larger populations.

CONCLUSION

- Psoriasis is a common chronic inflammatory dermatological disease present worldwide and causes significant morbidity. Its etiology is unknown, however it is generally thought that a complex autoimmune inflammatory disease with a genetic basis.
- Several studies put forward the fact, that psoriasis is by the Th17 cell–mediated disease which was driven by IL-23.
- There is increase in IL-23 values in cases when compare with controls as per many other studied.
- But in this study there is an insignificant relationship between cases and controls in IL-23 values.
- May be due to the study population is selected from low socioeconomic state people, have been relatively associated with elevated levels of inflammatory markers due to their lifestyle.

LIMITATIONS OF THE STUDY

This study has following limitations:

- The sample size is small.
- The fact that the hidden history of any exclusion factors may interfere in this study, may be due to poverty with illiteracy.
- Unawareness of psoriasis and no treatment for longer time or may be latent psoriasis.
- However, more analysis is required to demonstrate this theory. Currently as far as my opinion, there is no reliable data concerning the prevalence of psoriasis in the general population of India.

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Fig 1: World map showing the DALYs for psoriasis per 100 000, rates for all ages and both Sexes. Source: Adapted from IHME GBD 2010 (1).

Fig2: Early case of Psoriasis attended the Dermatology OP in KMC

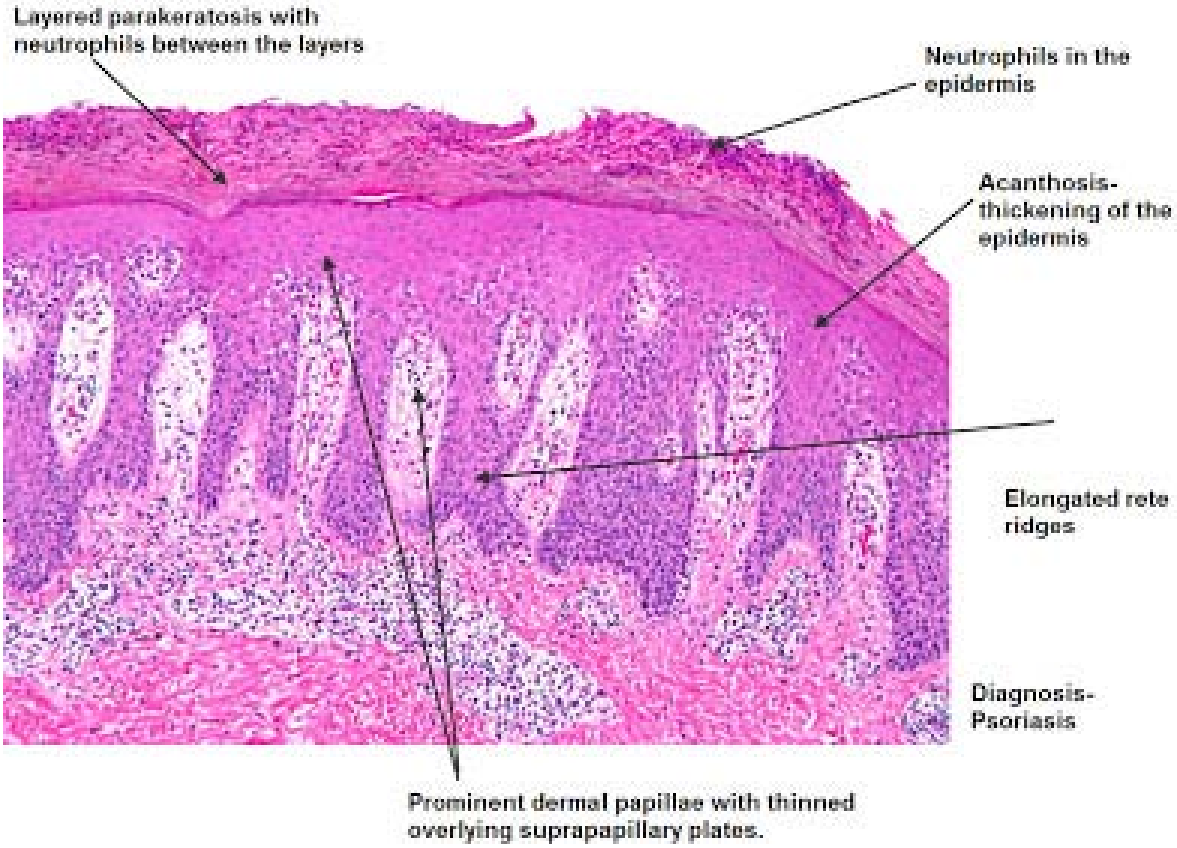


Fig 3: Microscopic structure of psoriasis- thinned stratum granulosum; extensive overlying parakeratotic scale; elongated dermal papillae with dilated capillaries inside;

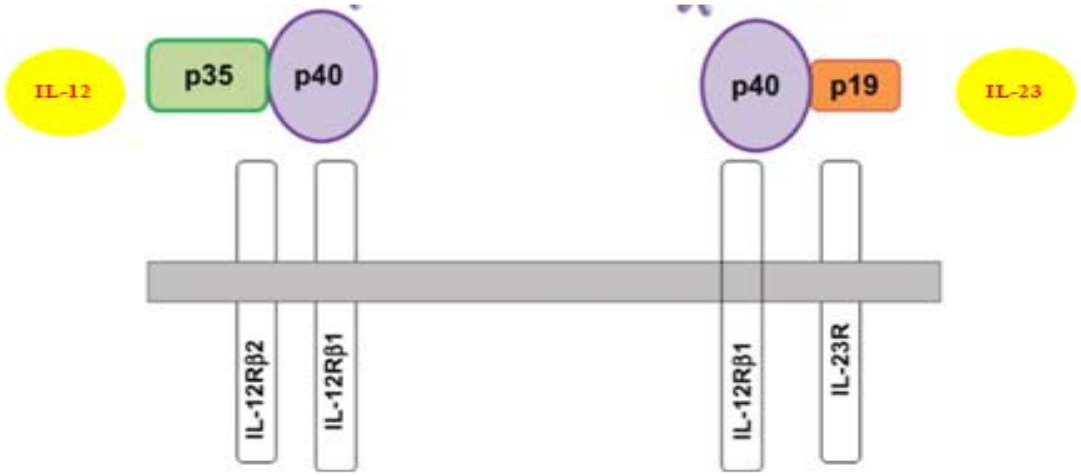


Fig 4: IL-23 and IL-12 structure and receptors. The IL-23 cytokine is compiled of 2 chains, p40 and p19, both are connected covalently and IL-12 composed of p35 and p19. p40 is shared by IL-23 and IL-12. IL-23 receptor consists of IL-12Rβ1 and IL-23R; the IL-12 receptor made of IL-12Rβ1 and IL-12Rβ2.

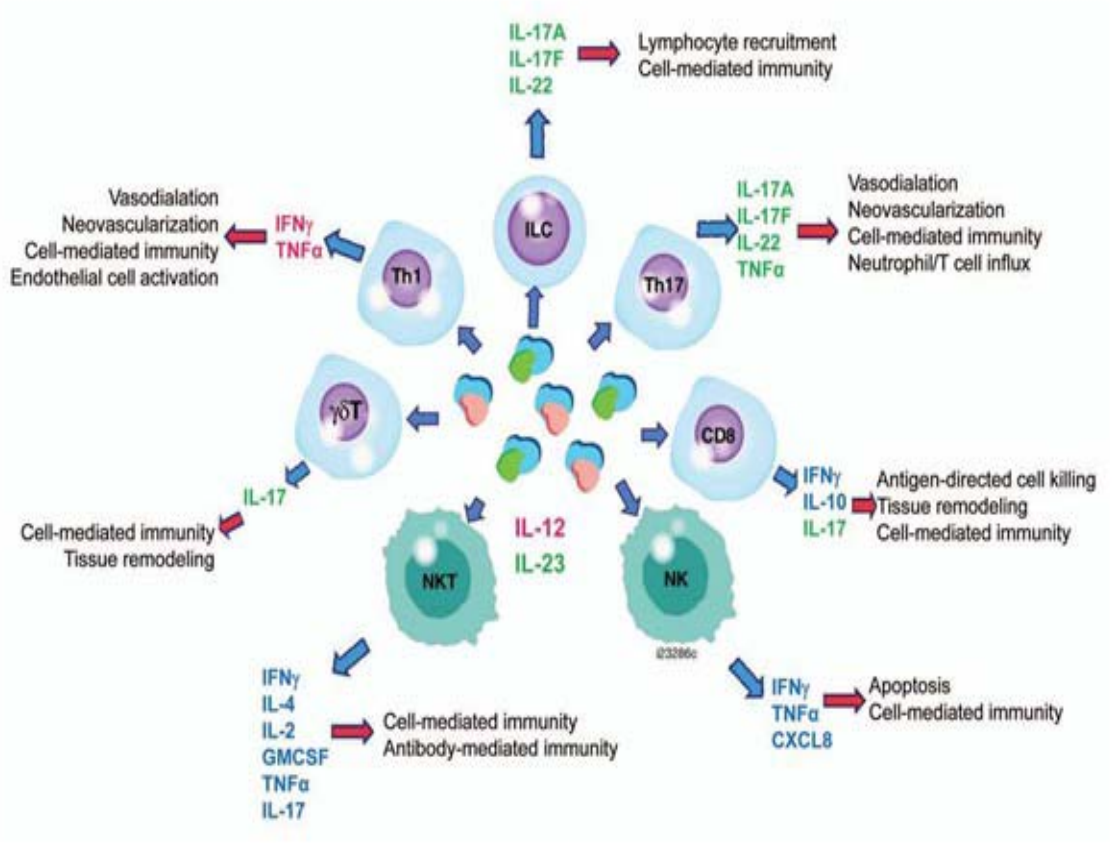


Fig 5: the functional comparison of IL23 and IL-12.

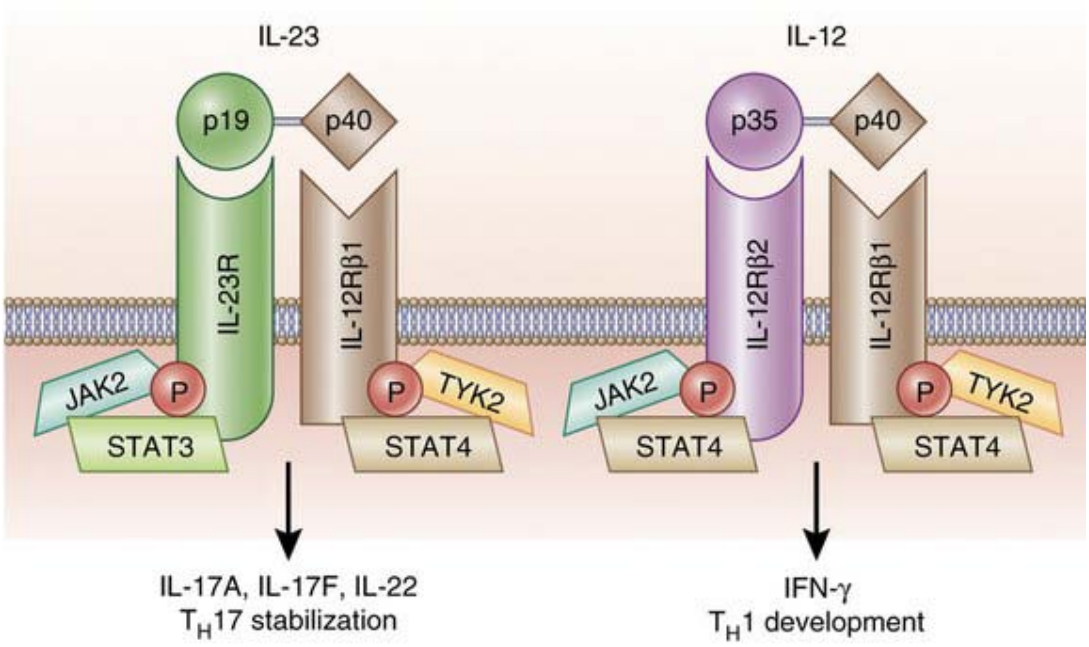


Figure 6: Schematic representation of IL-12 and IL-23, and their receptors and downstream signaling pathways.

IL-12 stimulation of JAK2 and TYK2 activity leads to phosphorylation of STAT4 and other STAT molecules. IL-23 also activates the JAK-STAT pathway but acts mainly on STAT3. IL-12 induces the production of IFN-γ, which is required for the development of T_H1 immune response. IL-23 induces IL-17A, IL-17F and/or IL-22 and stabilizes T_H17 cells.

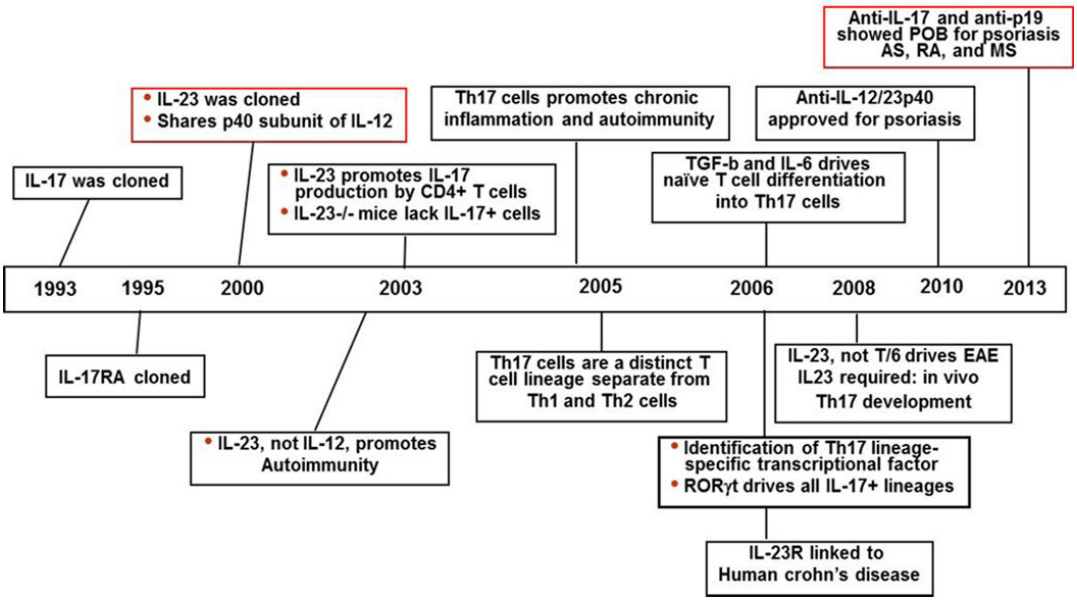


Fig 7: The discovery of IL-23/Th-17 immune pathway

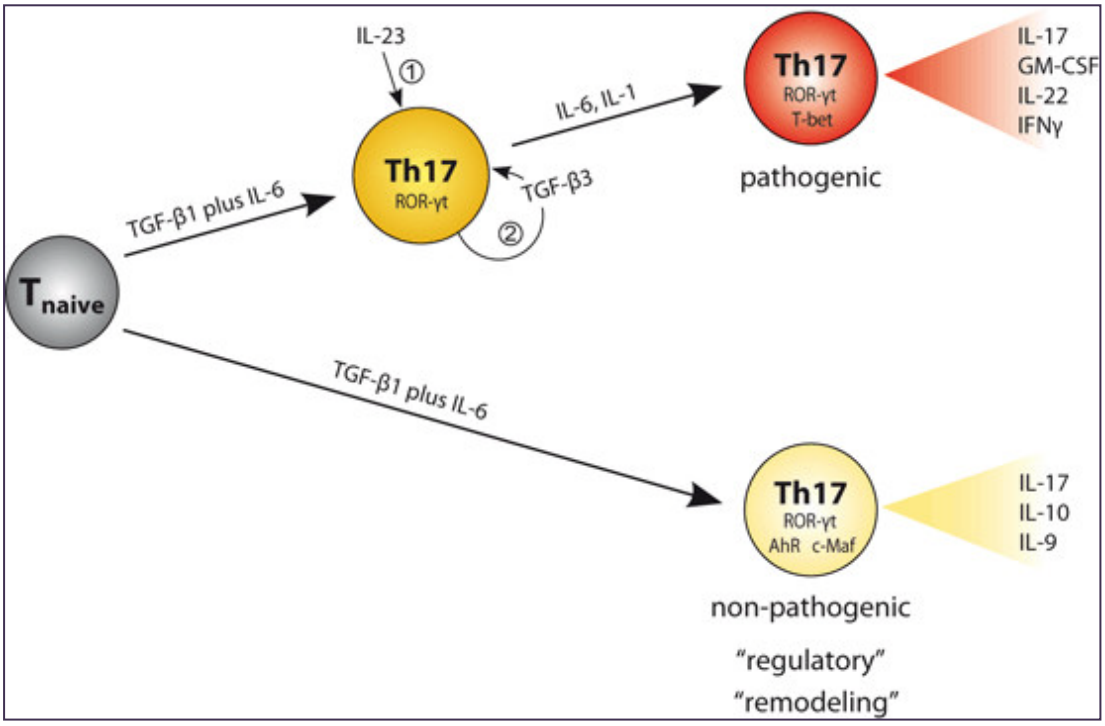


Fig 8: development and differentiation of Th17 cells

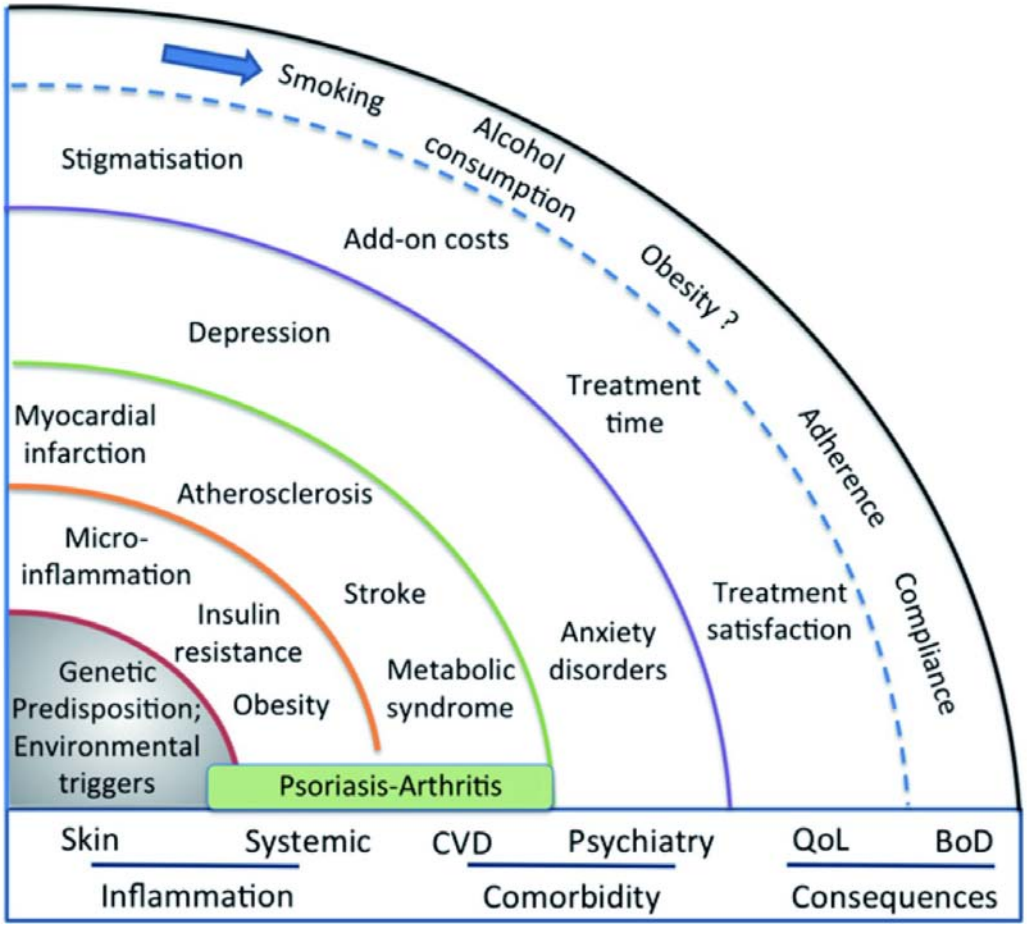
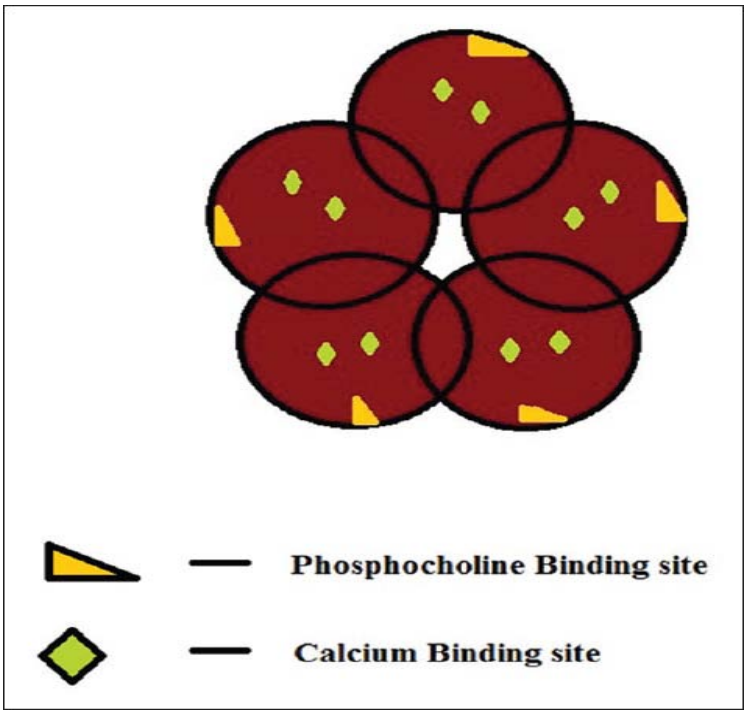


Fig 9 : co-morbidities and associations with psoriasis



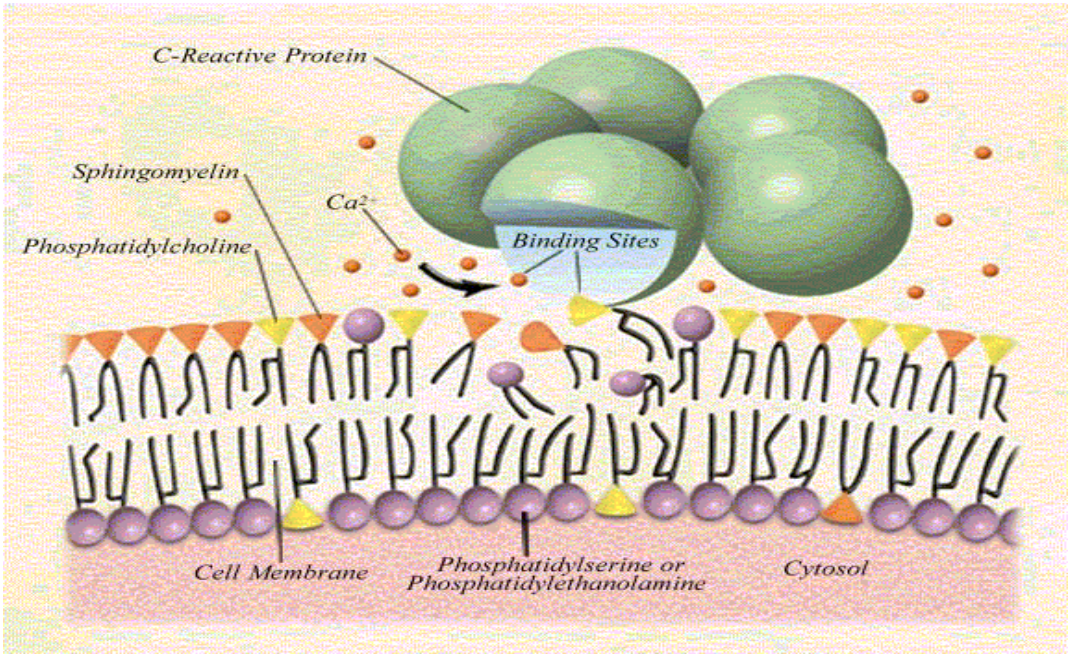
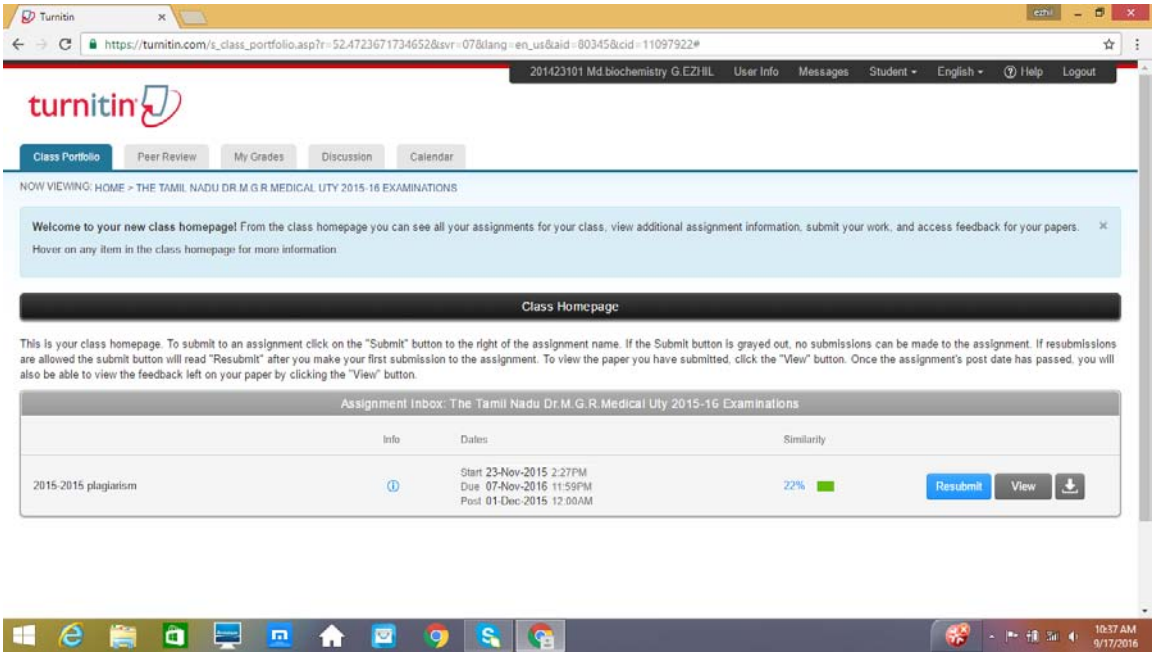


Fig 10 : Illustration showing the structure of C - Reactive protein representing the pentameric polypeptide subunits with 2 calcium binding sites and 1 binding site for phosphocholine.

Fig 11: Different types of cases attended the Skin OP in KMC, Chennai

ANNEXURE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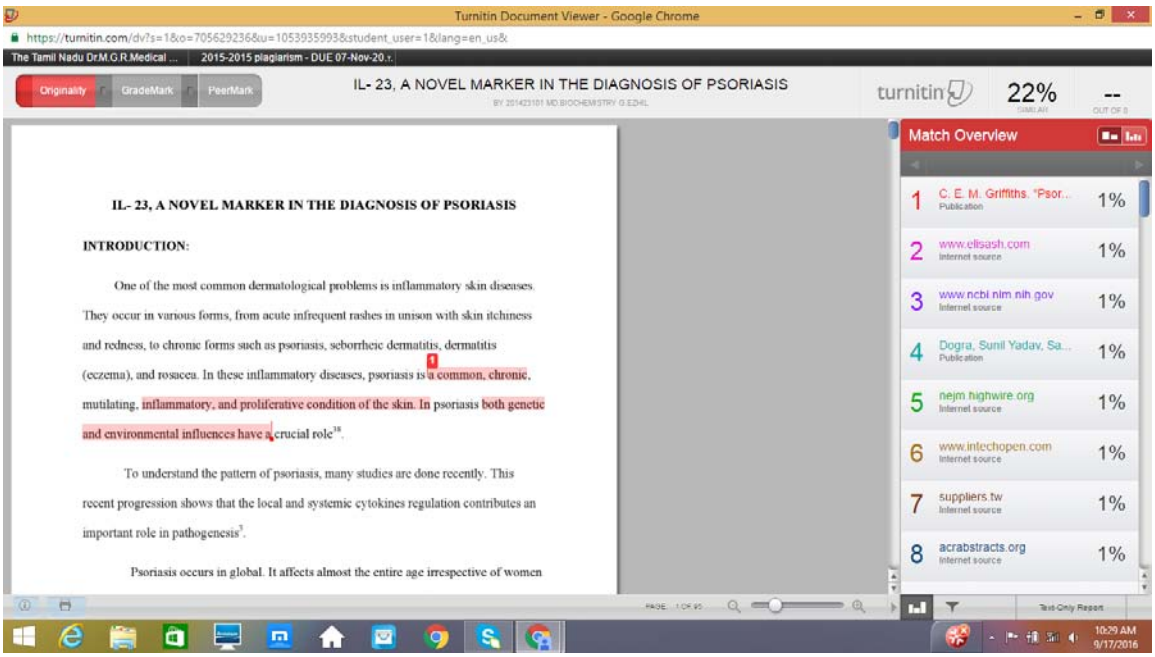
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INTRODUCTION:
One of the most common dermatological problems is inflammatory skin diseases. They occur in various forms, from acute infrequent rashes in unison with skin itchiness and redness, to chronic forms such as psoriasis, seborrheic dermatitis, dermatitis (eczema), and rosacea. In these inflammatory diseases, psoriasis is a common, chronic, mutilating, inflammatory, and proliferative condition of the skin. In psoriasis both genetic and environmental influences have a crucial role[38].
To understand the pattern of psoriasis, many studies are done recently. This recent progression shows that the local and systemic cytokines regulation contributes an important role in pathogenesis[3].
Psoriasis occurs in global. It affects almost the entire age irrespective of women
10:29 AM
9/17/2016

PATIENT CONSENT FORM

STUDY TITLE: IL-23, A NOVEL MARKER IN THE DIAGNOSIS OF PSORIASIS.

STUDY CENTRE: GOVT. KILPAUK MEDICAL COLLEGE HOSPITAL, CHENNAI-10

PATIENT'S NAME:

PATIENT'S AGE:

IDENTIFICATION NUMBER:

I confirm that I have understood the purpose and procedure of the above study. I have the opportunity to ask any questions and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in this study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that the sponsor of clinical study, working on sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However I understand that my identity would not be revealed in any information released to third parties unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical and radiological tests.

Signature/thumb impression :

Patient's name and address:

PROFORMA

NAME: **OP NO:**

AGE/SEX:

ADDRESS: **OCCUPATION:**

DATE:

PRESENT HISORY:

- The duration of psoriasis
- Any prior similar episodes or other skin diseases.

PAST HISTORY:

- History of liver/kidney disease.
- History of any respiratory diseases like tuberculosis.

PERSONAL HISTORY:

1) H/O Smoking. Alcohol intake.
2) H/O DM, HT, CAD, BONE DISEASES.
3) H/O inflammatory bowel disease.
4) H/O cancer.
5) H/O Other type of skin diseases like atopic dermatitis.
6) H/O drug intake for past 4 weeks.

FAMILY HISTORY:

1) H/O psoriasis.
2) H/O any autoimmune diseases.

ON EXAMINATION:

GENERAL EXAMINATION:

VITALS:

BP: **PULSE RATE:**

CVS: **RS:**

PER ABDOMEN: **CNS:**

INVESTIGATIONS:

1) Serum C-reactive protein: Quantitative Turbidimetric Test
2) Blood urea: UV- GLDH Method.
3) Serum Creatinine: JAFFE'S Kinetic Method.
4) Blood glucose random: Glucose Oxidase - Peroxidase Method.
5) Total and Differential Count: Electrical Impedance Method
6) Serum IL-23: ELISA Technique

MASTER CHART

SL.NO.	SEX	SUGAR	UREA	CREAT	TC	POLY	LYMPHO	EOSINO	MONOCYTE	BASOPHIL	CRP	IL-23
1	Female	77.85	26.46	0.566	10,300	84	12	1	3	0	3	46.23
2	Male	223.00	14.78	0.850	6,300	66	20	9	5	0	20	65.52
3	Male	67.59	14.56	0.861	5,700	48	48	2	2	0	13	153.80
4	Male	174.40	24.13	1.097	7,000	54	43	3	4	0	6	138.90
5	Male	91.66	28.12	0.753	6,800	43	50	3	4	0	5	141.30
6	Male	74.11	20.85	0.756	10,300	67	23	5	5	0	7	105.20
7	Male	222.40	16.72	0.853	6,300	60	28	8	4	0	7	67.32
8	Female	231.30	16.65	0.581	5,500	58	33	5	4	0	6	90.36
9	Female	255.10	9.60	0.714	6,600	52	25	19	4	0	8	33.76
10	Male	154.50	18.09	0.756	6,300	45	47	4	4	0	6	39.34
11	Female	100.40	17.08	0.698	5,900	57	33	4	6	0	14	45.30
12	Female	351.00	14.24	0.735	6,300	59	29	6	4	0	15	50.86
13	Male	103.70	12.15	0.929	7,000	54	37	3	4	0	5	50.51
14	Female	108.10	12.76	0.704	9,700	66	27	4	3	0	17	34.66
15	Female	97.91	16.97	0.690	7,400	62	33	3	2	0	12	68.62
16	Female	122.30	14.92	0.757	9,600	63	30	4	3	0	7	115.90
17	Female	103.40	16.11	0.787	8,700	54	38	6	2	0	1	39.46
18	Male	101.60	16.18	1.028	9,300	67	20	8	5	0	6	42.21
19	Female	98.86	26.97	0.891	8,200	40	48	4	5	0	0	39.57
20	Male	235.90	29.34	0.982	9,200	51	41	4	4	0	6	50.56
21	Female	129.70	13.63	0.772	5,600	60	34	3	3	0	8	36.15
22	Female	350.50	21.97	0.871	6,800	47	42	6	5	0	6	71.71
23	Female	89.33	19.60	0.757	8,600	62	31	2	5	0	9	57.03
24	Female	132.80	13.52	0.569	5,600	46	36	13	5	0	10	60.76
25	Female	105.00	10.50	0.743	9,600	52	42	3	3	0	4	65.53
26	Female	103.50	16.29	0.700	5,100	49	45	2	4	0	11	39.63
27	Female	60.16	15.07	0.734	5,100	50	40	4	4	0	7	53.57
28	Male	94.97	20.78	0.902	7,400	63	30	3	4	0	9	54.61

29	Male	99.22	18.27	0.947	5,500	57	35	2	6	0	4	59.80
30	Female	83.44	10.13	0.703	7,600	65	29	2	4	0	10	84.16
31	Female	107.70	33.94	1.008	8,100	61	33	2	4	0	4	75.29
32	Female	204.70	16.47	0.953	9,300	63	27	6	4	0	13	68.44
33	Female	71.46	15.87	0.992	5,900	62	28	7	3	0	4	68.88
34	Male	78.48	34.66	0.872	9,100	66	25	3	6	0	7	38.47
35	Male	79.90	17.35	1.393	6,100	58	231	6	5	0	12	35.32
36	Male	68.21	15.35	1.070	8,700	56	33	6	5	0	5	74.09
37	Male	103.70	24.62	1.010	5,300	67	25	3	5	0	6	43.93
38	Male	133.80	16.09	0.827	7,000	51	42	2	5	0	9	36.68
39	Female	120.50	18.98	0.755	9,700	53	35	5	4	0	1	55.57
40	Female	98.33	43.12	0.958	6,700	40	44	12	4	0	14	71.03
41	Female	112.16	23.24	0.698	9,800	60	33	3	4	0	4	25.85
42	Female	104.83	21.80	0.738	6,100	63	34	6	6	0	20	28.37
43	Female	84.92	17.39	0.800	9,400	62	29	4	6	0	10	57.80
44	Female	95.60	16.07	0.602	5,700	46	33	10	5	0	8	36.32
45	Female	102.85	20.65	0.782	6,200	56	31	3	5	0	3	83.61
46	Female	130.80	27.90	0.675	7,500	66	27	2	5	0	5	90.51
47	Female	148.60	18.99	0.762	7,200	64	31	2	3	0	6	67.40
48	Female	130.70	19.96	0.693	7,400	53	38	4	5	0	6	60.00
49	Female	117.40	14.85	0.677	6,000	68	26	2	4	0	6	64.26
50	Female	174.50	20.39	0.837	7,400	57	34	6	3	0	4	60.55
51	Male	154.40	24.48	1.292	6,800	57	35	4	4	0	7	56.00
52	Male	129.10	21.18	0.917	11,800	62	27	8	3	0	9	62.36
53	Male	154.20	21.32	0.853	8,800	71	25	2	5	0	3	51.80
54	Female	179.20	21.75	0.730	10,700	70	25	3	2	0	13	33.37
55	Female	133.30	16.18	0.825	6,300	56	38	3	3	0	6	58.72
56	Female	223.10	16.54	0.847	9,400	48	35	15	2	0	3	54.80
57	Female	159.00	18.05	0.900	8,600	61	35	2	5	0	5	62.10
58	Female	104.30	17.69	1.070	9,500	62	29	5	4	0	7	45.90
59	Female	99.75	20.24	0.759	6,700	66	28	2	4	0	5	54.32

60	Female	88.99	14.89	0.884	5,200	58	33	3	6	0	11	62.00
61	Female	160.90	17.69	0.800	6,700	56	36	4	4	0	10	50.60
62	Female	120.60	18.77	1.058	7,900	50	43	4	3	0	5	31.28
63	Female	121.70	31.93	0.912	6,200	51	38	6	5	0	11	75.45
64	Male	108.60	17.87	0.944	9,900	42	33	22	3	0	17	48.85
65	Female	118.80	15.93	0.680	5,100	46	48	2	4	0	6	47.90
66	Female	108.80	23.80	0.774	4,300	45	33	2	3	0	14	65.46
67	Female	97.24	13.56	0.993	10,600	66	26	3	5	0	8	54.48
68	Female	116.30	13.88	0.756	7,000	64	32	2	2	0	6	81.01
69	Female	86.55	16.50	0.688	6,400	57	36	2	5	0	9	58.50
70	Female	89.00	14.00	0.800	8,000	61	35	2	2	0	21	62.25
71	Female	86.86	19.42	0.921	8,200	64	23	11	2	0	4	30.78
72	Female	93.81	20.06	0.772	6,600	66	27	4	3	0	7	54.15
73	Female	111.70	13.34	0.978	5,200	51	43	2	4	0	6	42.67
74	Female	103.60	17.76	0.925	10,300	59	28	9	4	0	6	39.60
75	Female	192.10	25.13	0.575	9,100	76	18	2	4	0	11	63.13
76	Female	110.90	13.12	0.773	6,700	65	30	3	6	0	5	87.90
77	Female	83.67	19.02	0.953	11,300	62	31	4	3	0	10	210.03
78	Female	78.81	13.81	0.642	8,900	67	28	1	4	0	5	60.65
79	Male	130.40	18.36	0.912	9,200	63	31	2	4	0	5	202.96
80	Male	175.60	24.85	0.977	8,000	65	27	2	6	0	5	56.80
81	Female	106.80	16.90	0.812	6,200	55	39	3	3	0	5	73.55
82	Female	115.30	24.67	0.838	6,300	68	25	4	6	0	6	35.55
83	Male	354.30	25.35	1.479	6,700	60	35	3	2	0	11	94.90
84	Male	342.90	22.19	1.461	6,800	56	40	2	6	0	8	67.90
85	Female	357.50	14.35	0.760	8,500	63	32	3	2	0	9	68.27
86	Female	89.05	9.03	0.854	5,700	64	33	1	2	0	8	96.63
87	Male	90.71	17.98	1.147	6,100	40	52	3	5	0	5	69.71
88	Female	102.90	20.64	0.882	7,000	56	38	3	3	0	3	195.83
89	Female	115.40	17.98	0.780	10,400	66	30	2	6	0	22	182.50
90	Female	85.18	15.68	0.659	4,100	52	41	3	4	0	4	116.80

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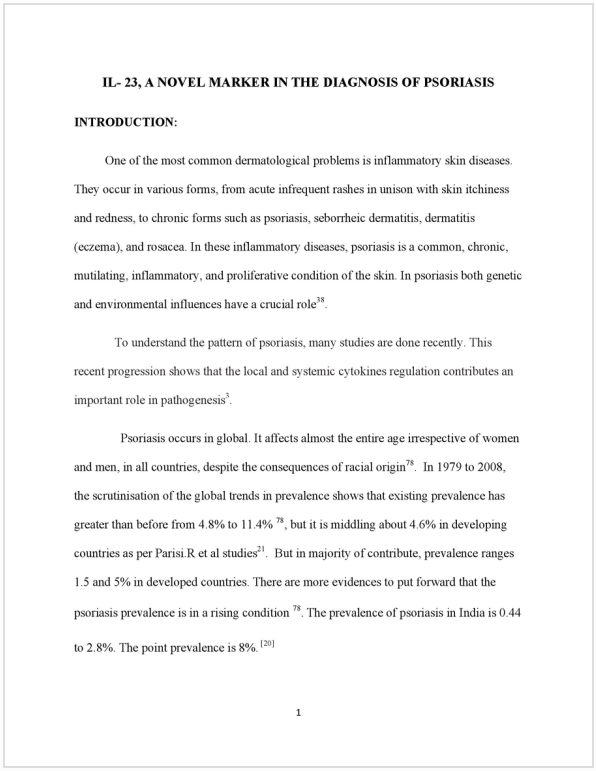

IL- 23, A NOVEL MARKER IN THE DIAGNOSIS OF PSORIASIS

INTRODUCTION:

One of the most common dermatological problems is inflammatory skin diseases. They occur in various forms, from acute infrequent rashes in unison with skin itchiness and redness, to chronic forms such as psoriasis, seborrheic dermatitis, dermatitis (eczema), and rosacea. In these inflammatory diseases, psoriasis is a common, chronic, mutilating, inflammatory, and proliferative condition of the skin. In psoriasis both genetic and environmental influences have a crucial role[38].

To understand the pattern of psoriasis, many studies are done recently. This recent progression shows that the local and systemic cytokines regulation contributes an important role in pathogenesis[5].

Psoriasis occurs in global. It affects almost the entire age irrespective of women and men, in all countries, despite the consequences of racial origin[78]. In 1979 to 2008, the scrutinisation of the global trends in prevalence shows that existing prevalence has greater than before from 4.8% to 11.4% [78], but it is middling about 4.6% in developing countries as per Parisi.R et al studies[21]. But in majority of contribute, prevalence ranges 1.5 and 5% in developed countries. There are more evidences to put forward that the psoriasis prevalence is in a rising condition [78]. The prevalence of psoriasis in India is 0.44 to 2.8%. The point prevalence is 8%.[20]

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INSTITUTIONAL ETHICS COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID. No. 5/2016 Dt: 11.02.2016
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "IL – 23, a novel marker in the Diagnosis of psoriasis" - For Project Work submitted by Dr.G.Ezhil, PG MD (Bio-Chem), Govt. Kilpauk Medical College, Ch – 10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

DEAN. 24/2/11
Govt.Kilpauk Medical College,
Chennai – 10.

நோயாளி ஒப்புதல் படிவம்

ஆராய்ச்சியின் விவரம்:

ஆராய்ச்சி மையம்:

நோயாளியின் பெயர்: நோயாளியின் வயது:

பதிவு எண்:

நோயாளி கீழ்கண்டவற்றுள் கட்டங்களை (✓) செய்யவும்

1. மேற்குறிப்பிட்டுள்ள ஆராய்ச்சியின் நோக்கத்தையும் பயனையும் முழுவதுமாக புரிந்துகொண்டேன். மேலும் எனது அனைத்து சந்தேகங்களையும் கேட்டு அதற்கான விளக்கங்களையும் தெளிவுபடுத்திக் கொண்டேன். ☐

2. மேலும் இந்த ஆராய்ச்சிக்கு எனது சொந்த விருப்பத்தின் பேரில் பங்கேற்கிறேன் என்றும், மேலும் எந்த நேரத்திலும் எவ்வித முன்னறிவிப்புமின்றி இந்த ஆராய்ச்சியிலிருந்து விலக முழுமையான உரிமை உள்ளதையும், இதற்கு எவ்வித சட்ட பிணைப்பும் இல்லை என்பதையும் அறிவேன். ☐

3. ஆராய்ச்சியாளரோ, ஆராய்ச்சி உதவியாளரோ, ஆராய்ச்சி உபயத்தாரோ, ஆராய்ச்சி பேராசிரியரோ, ஒழுங்குநெறி செயற்குழு உறுப்பினர்களோ எப்போது வேண்டுமானாலும் எனது அனுமதியின்றி எனது உள்நோயாளி பதிவுகளை இந்த ஆராய்ச்சிக்காகவோ அல்லது எதிர்கால பிற ஆராய்ச்சிகளுக்காகவோ பயன்படுத்திக்கொள்ளலாம் என்றும், மேலும் இந்த நிபந்தனை நான் இவ்வாராய்ச்சியிலிருந்து விலகினாலும் தகும் என்றும் ஒப்புக்கொள்கிறேன். ஆயினும் எனது அடையாளம் சம்பந்தப்பட்ட எந்த பதிவுகளும் (சட்டபூர்வமான தேவைகள் தவிர) வெளியிடப்படமாட்டாது என்ற உறுதிமொழியின் பெயரில் இந்த ஆராய்ச்சியிலிருந்து கிடைக்கப்பெறும் முடிவுகளை வெளியிட மறுப்பு தெறிவிக்கமாட்டேன் என்று உறுதியளிக்கின்றேன். ☐

4. இந்த ஆராய்ச்சிக்கு நான் முழுமனதுடன் சம்மதிக்கின்றேன் என்றும் மேலும் ஆராய்ச்சிக் குழுவினர் எனக்கு அளிக்கும் அறிவுரைகளை தவறாது பின்பற்றுவேன் என்றும் இந்த ஆராய்ச்சி காலம் முழுவதும் எனது உடல் நிலையில் ஏதேனும் மாற்றமோ அல்லது எதிர்பாராத பாதகமான விளைவோ எற்படுமாயின் உடனடியாக ஆராய்ச்சி குழுவினரை அணுகுவேன் என்றும் உறுதியளிக்கின்றேன். ☐

5. இந்த ஆராய்ச்சிக்குத் தேவைப்படும் அனைத்து மருத்துவப் பரிசோதனைகளுக்கும் ஒத்துழைப்பு தருவேன் என்று உறுதியளிக்கின்றேன். ☐

6. இந்த ஆராய்ச்சிக்கு யாருடைய வற்புருத்தலுமின்றி எனது சொந்த விருப்பத்தின் பேரிலும் சுயஅறிவுடனும் முழுமனதுடனும் சம்மத்திக்கின்றேன் என்று இதன் மூலம் ஒப்புக்கொள்கிறேன். ☐

நோயாளியின் கையொப்பம் / பெருவிரல் கைரேகை ஆராய்ச்சியாளரின் கையொப்பம்

இடம்: தேதி: